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PENICILLIN TREATMENT OF PNEUMOCOCCUS MENINGITIS IN INFANTS

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THE employment of penicillin as a new agent in the treatment of pneumococcus meningitis calls for a re-evaluation of the prognosis and a discussion of the therapeutic problems involved. Previous reports on the use of penicillin in this formidable disease have dealt chiefly with adults or older children,[1-4] except for the recent article by Waring and Smith[5] and individual case reports.

Fourteen cases of pneumococcus meningitis in children under 2 years of age were treated with penicillin in the Infants' and Children's Hospitals between Sept. 20, 1943, and Dec. 28, 1944. It is the purpose of this study to present an analysis of these cases in an attempt to evaluate this form of therapy. The series is admittedly small and the results not entirely conclusive, inasmuch as the patients deserve a longer period of follow-up before it can be said to what extent they may be considered normal individuals and therefore cured.

The cases presented here serve to emphasize the problems which one encounters in the treatment of this type of meningitis in the infant age group, particularly in infants under 1 year. A few years ago the mortality rate for pneumococcus meningitis was practically 100 per cent for all ages. Specific antiserum combined with sulfonamides brought about an encouraging number of recoveries in children over 2 years of age[6] and in adults, but only rarely did an infant survive[7] (Fig. 1). Why this should be is not entirely clear. Several observations concerning the immunologic status of infants suggest not only a greater susceptibility[8] but also a lack of antigenic response[9] of infants to pneumococcus infections.

MATERIAL

The patients chosen for this study are those of the infant age group, that is, under 2 years. They fall into three categories: complete cures, bacteriologic cures (with residual damage), and deaths. Four older children were treated

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with penicillin in this hospital during the same period, of whom three recovered and one died—the latter being a child of 35 months who had had meningitis, with essentially no specific therapy, for two weeks before admission. The ages of the patients under consideration here varied from 6 weeks to 13 months. The age distribution shows a significant number of young infants, that is, under 6 months of age, in the entire group who were treated with penicillin.

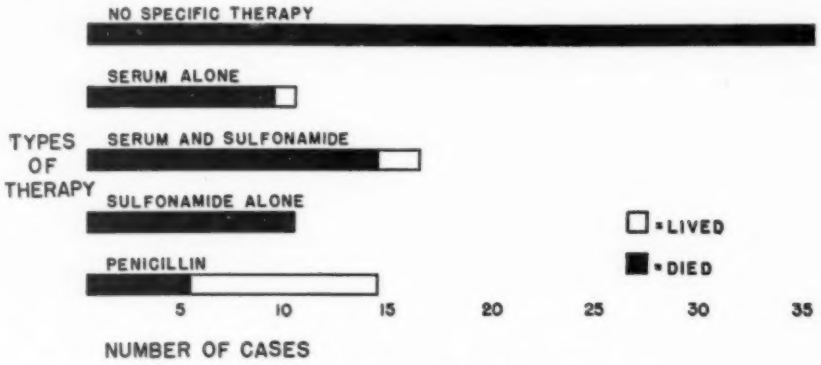

Fig. 1.—Pneumococcus meningitis in infants, 1930-1944.

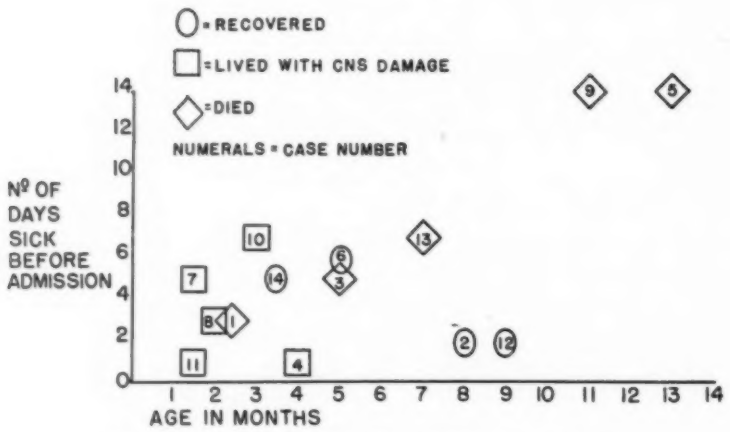

Fig. 2.—Pneumococcus meningitis; penicillin-treated infants.

A variety of factors contributed to the final outcome of these cases. Chief among them were: (1) the age of the patient, and (2) the length of time the patient had presumably had meningeal infection prior to admission. It was often difficult to determine the second factor accurately from the histories elicited. In general, symptoms referable to the central nervous system, although not necessarily specific for meningeal infection, were taken as the time of onset of the meningitis. These symptoms consisted of listlessness and irritability (subsequent

to signs of upper respiratory infection and fever), convulsions or twitchings, unresponsiveness, stiffness of the neck, and bulging anterior fontanel—each of which was noted by the parents or the referring physician. They determine the time of onset shown in Fig. 2 and therefore the "number of days sick before admission." Further analysis will include such items as: therapy prior to admission; severity of the infection as judged by the general condition of patient and the spinal fluid findings on admission; and therapy in this hospital.

CLINICAL FINDINGS

As already mentioned, it was not always possible from the histories to fix an accurate time of onset of the meningitis. In eleven cases there was a history of an upper respiratory infection within two weeks of admission, one patient was said to have had pneumonia twelve days before, and one "pneumonia of both lungs" five days before admission. The last (Case 6) was the next to the youngest infant to make a good recovery. She had pneumonia again during her convalescence from meningitis and was readmitted for pneumonia two months later.

The appearance of all the patients at the time of admission was sufficiently alarming to warrant immediate lumbar punctures. Eight of the fourteen had initial temperatures of 101 to 103° F., four had higher, and two had nearly normal temperatures but developed fever within eight hours. All of the patients were semicomatose or completely so on admission and some had twitching, convulsive movements. A tense or bulging anterior fontanel was a prominent sign in eight. Foci of infection in the respiratory system were not in themselves alarming. Five patients had some catarrhal otitis media and ten had various degrees of pharyngeal infection. X-ray evidence of some pneumonic infiltration was present in three patients, but clinically the pneumonia was severe only in Case 12. The signs pointing to meningeal irritation—in addition to the state of consciousness—were: hyperactive knee and ankle jerks in ten cases, stiff neck in nine, and a positive Kernig and other abnormal reflexes in five. In general, the physical examinations illustrated how variable the signs of meningitis are in infants.

LABORATORY

The first specimen of spinal fluid presented unquestionable evidence of meningitis in each case. The number of cells varied from 88 per cubic millimeter to cells too numerous to count in undiluted fluid. The pressure (by observation of the rate of flow only) was elevated in five of the cases, and the sugar content (per drop of cerebrospinal fluid in Benedict's qualitative reagent) decreased in eleven of the fourteen. In all but one case it was possible to type the pneumococci within one or two hours, directly from the spinal fluid obtained on the first lumbar puncture. In that one case the organisms were typed the next day from the culture of the initial fluid. The pneumococcus types determined thus, and in eleven cases from confirmatory positive blood cultures, were: one, type I; three, type V; two, type VI; one, type VII; one, type IX; one, type XII; two, type XIV; one, type XVIII; one, type XIX; and one, type XXVII. The blood

TABLE I

CASE	ADMISSION DATE	NAME AGE SEX	DAYS SICK BEFORE ADMISSION (NO.)	CONDITION ON ADMISSION	PREVIOUS THERAPY	SPINAL FLUID	HOSPITAL THERAPY	OUTCOME	REMARKS
1	9/20/43	K. S. 2 mo. F	4	"Appears acutely ill"; fontanel slightly tense; temperature 103.8° F.	None	Pneumococcus XXVII; 510 white blood cells; culture sterile in two days	Sulfadiazine for 2 days, penicillin 9 days I.T.; penicillin 14 days I.M.; anti-serum 98,000 units I.V.	Died 12/24/43	Discharged with CNS damage; died 2 mo. later
2	10/18/43	A. C. 8 mo. F	2	Comatose; few twitchings; bulging fontanel; temperature 99.4 to 102° F.	None	Pneumococcus VI; 36,000 white blood cells; culture sterile in 1 day	1 dose sodium sulfadiazine s.c.; penicillin 4 days I.T.; penicillin 8 days I.M.	Recovered	Temporary residual weakness of one hand
3	11/11/43	J. R. 5 mo. M	5	Semistuporous, spastic, twitching; fontanel soft; temperature, 102° F.	Sulfadiazine for 5 days before admission	Pneumococcus IV; 88 white blood cells; culture sterile in 24 hr. then positive three times later	Penicillin 12 days I.T.; then for 3 days I.T., starting eighteenth hospital day; penicillin 23 days I.M.	Died 12/5/43	Obstructive hydrocephalus, sinus thrombosis, pneumococcemia and typhimurium bacteremia at postmortem
4	11/26/43	J. W. 4 mo. M	1	Cyanotic; "convulsive jerking"; fontanel slightly tense; temperature, 106° F.	None	Pneumococcus XIV; 1,600 white blood cells; culture sterile in 1 day	1 dose sodium sulfadiazine s.c.; penicillin 8 days I.T.; penicillin 9 days I.M.	Lived with CNS damage	Spinal fluid block; catheter irrigation of basal cistern
5	12/15/43	E. D. 13 mo. F	14	"Completely stuporous"; irregular breathing; temperature, 99.2 to 104° F.	Sulfadiazine twice for a few days each	Pneumococcus XIX; 175 white blood cells and fibrin; culture sterile in 2 days	Sodium sulfadiazine 2½ days s.c.; penicillin 3 days I.T.; penicillin 5 days I.M.; anti-serum 100,000 units I.V.; oxygen I.T.	Died	Dilated ventricles (pneumoencephalogram on fifth hospital day)

6	12/18/44	B. T. 5 mo. F	5	Listless; high-pitched cry; fontanel flat; temperature, 103° F.	Sulfamerazine for 5 days	Pneumococcus IX; 2,470 white blood cells; culture sterile in 1 day	1 dose sodium sulfadiazine s.c.; sulfadiazine 1 day p.o.; penicillin 6 days I.T.; penicillin 9 days I.M.; oxygen 6 days I.T.	Recovered	Sulfadiazine for 5 days starting twentieth hospital day for bronchopneumonia
7	1/22/44	G. F. 6 weeks F	5	Irritable, pale, trembling; fontanel tense; temperature 101.8° F.	4 doses sulfadiazine 3 days before admission	Pneumococcus V; 1,200 white blood cells; culture sterile in 1 day	1 dose sodium sulfadiazine s.c.; penicillin 16 days I.T.; penicillin 5 days I.M.	Lived	Arrested hydrocephalus; development good
8	1/24/44	E. R. 7 weeks F	3	"Semiconscious," cyanotic; dyspneic; fontanel slightly tense; temperature, 102.4° F.	None	Pneumococcus VII; 8,400 white blood cells; culture sterile in 3 days	sulfadiazine for 7 days starting fourteenth hospital day and for 9 days starting forty-first day; penicillin 7 days I.T.; penicillin 13 days I.M.	Lived	Severe CNS damage; hydrocephalus; transferred to neurosurgery
9	2/ 3/44	P. L. 11 mo. M	14	Comatose; rigid; fontanel depressed; temperature 105° F.	Sulfadiazine p.o. for 2 weeks	Pneumococcus VI; 8,000 white blood cells; culture positive in 2 L.P.'s before I.T. penicillin	Penicillin 1 dose I.T.; Penicillin 1 day I.M.	Died in 36 hours	Separated skull sutures (by x-ray)
10	3/18/44	D. D. 3 mo. F	7	Pale, rigid with shallow respirations; bulging fontanel; temperature 101.8° F.	Sulfadiazine for 4 days	Pneumococcus V; 650 white blood cells; culture sterile in 1 day	Sodium sulfadiazine 3 days s.c.; sulfadiazine 22 days p.o.; penicillin 7 days I.T.; oxygen I.T.	Lived	Severe brain damage; institutionalized

TABLE I—CONT'D

CASE	ADMISSION DATE	NAME AGE SEX	DAYS SICK BEFORE ADMISSION (NO.)	CONDITION ON ADMISSION	PREVIOUS THERAPY	SPINAL FLUID	HOSPITAL THERAPY	OUTCOME	REMARKS
11	4/24/44	J. L. 6 weeks M	1	Drowsy; Cheyne-Stokes' respirations; fontanel flat; temperature, 101.8° F.	None	Pneumococcus V; 700 white blood cells; culture sterile in 1 day	Penicillin 11 days I.T.; penicillin 12 days I.M.; oxygen I.T.	Lived	Mentally retarded at 9 mo. follow-up
12	11/ 2/44	J. J. M. 9 mo. M	2	Acutely ill; hydrocephalic (congenital); signs of pneumonia; fontanel tense; temperature 103.6° F.	Sulfadiazine 1 day	Pneumococcus XIV; no cells at first	Sulfadiazine or sodium sulfadiazine for 3 days, penicillin for 24 days I.M. plus sulfadiazine 19 days; penicillin 9 days I.T. starting 11/13/44	Recovered	Congenital hydrocephalic who developed meningitis in hospital in course of pneumonia
13	12/19/44	J. J. D. 7 mo. M	5	Comatose, shrill cry; fontanel soft; temperature 102° F.	None	Pneumococcus XII; 3,000 white blood cells	Sodium sulfadiazine I.V. and s.c.; penicillin 2 times I.T.; penicillin 1 day I.M.; antiserum 60,000 units I.V.	Died in 24 hours	? Head injury 2 days before onset of symptoms
14	12/28/44	A. M. 3½ mo. F	4	Irritable, not acutely ill; fontanel slightly full; temperature 102.2° F.	Sulfadiazine for 4 days	Pneumococcus XVIII; 800 white blood cells; culture sterile in 16 hours	Sodium sulfadiazine 20 days s.c.; penicillin 12 days I.T.; penicillin 13 days I.M.; antiserum 60,000 units I.M.	Recovered	

Key: I.V. = Intravenously; I.M. = Intramuscularly; I.T. = Intrathecally; s.c. = Subcutaneously; T. = Temperature (Fahrenheit); p.o. = by mouth; CNS = central nervous system.

cultures that proved to be sterile were obtained from patients who had been treated with a sulfonamide before admission.

Routine nose and throat cultures were done on all but one of the patients and showed pneumococci to be present in six of the fourteen cases. The admission white blood counts ranged from 4.25 thousand to 47.8 thousand, and all but three of these were above 14 thousand. The latter three rose considerably above normal within the first week. In these lower counts only was there a lymphocytic rather than a polymorphonuclear preponderance in the differential.

THERAPY

Seven of the fourteen patients had had some form of sulfonamide at various intervals before hospitalization. The indications were usually described as sore throat or pneumonia, but in one case pneumococcus meningitis was known to be present. In at least four of them the dosage schedule was too low for the treatment of a severe infection.

The therapy in this hospital, while fundamentally similar in all these cases, was varied from time to time for special reasons. Three of the patients appeared so ill at the time of admission that they were given single doses of intravenous sodium sulfadiazine as soon as the lumbar puncture and blood culture had been done. In six other patients either parenteral or oral sulfadiazine was given at various times throughout the course of the illness for complications or for reasons associated with the meningitis which will be discussed later. If sulfadiazine was used, an attempt was made to keep the blood levels above 12 and preferably between 15 and 20 mg. per cent in the early course of therapy.

Penicillin was given intramuscularly on a dosage schedule of 3,000 units every three hours in the earlier cases and smaller infants. The other patients were given 5,000 units every three hours. The schedule of intrathecal therapy was 10,000 units twice a day (or three times a day for the first few days), in an aqueous or saline solution containing 1,000 units per cubic centimeter. In the earlier cases the dosage was somewhat less, 2,500 to 5,000 units two or three times a day. The dosage sometimes departed from this schedule because of mechanical difficulties encountered which limited the amount of spinal fluid removed. When blocks occurred so that spinal fluid could not be obtained by the lumbar route, penicillin was given intracisternally when possible, and, in a few cases, intraventricularly. Penicillin was administered by the intrathecal route for an average of eleven days, but the extremes were from 1 to 16 days. In some cases it was given intermittently because of the mechanical difficulties already mentioned, and in one because of a recurrence of positive spinal fluid cultures. The latter patient (Case 3) died with a complicating infection.

In four of the cases an attempt was made to replace most of the spinal fluid with oxygen in the hope of lessening the formation of subarachnoid adhesions. The results in the individual cases may be seen from Table I. The data are insufficient for an evaluation of this procedure.

Type-specific antipneumococcus rabbit serum was given in four of the cases (Cases 1, 5, 13, and 14). The indications were: uncertainty concerning the

effectiveness of penicillin therapy in the first case, the severity of the infection in the second, and the youth of the patients and previous disappointing results with penicillin in the remaining two.

RESULTS

There were four apparently complete cures, five recoveries in which the children were left with varying degrees of central nervous system damage, and five deaths. In Fig. 2 the cases are charted with reference to the age of the patient and the length of time he or she had been sick before admission. It is clear that, even in the older infants, when meningitis had been present for one or two weeks before penicillin was started, the prognosis was extremely poor. Evidently infants under 5 months of age, even when penicillin therapy is instituted within the first week of illness, have small chance of escaping some permanent central nervous system damage. The damage seemed to arise from the toxic effect on cerebral cells, secondary destruction of cerebral tissue as the result of pressure from obstructive hydrocephalus, and possibly thrombosis of nutrient blood vessels.

Two infants were only 6 weeks old, and both recovered with residual central nervous system damage. One (Case 7), who has moderate internal hydrocephalus, is developing fairly well (that is, sat alone at 8 months, started to pull to a standing position at 11 months). The other (Case 11), who had had a previous admission for neonatal intracranial hemorrhage, is in an excellent state of nutrition but is retarded in motor development. There was one infant 7 weeks old (Case 8) who had a severe complicating hydrocephalus and had a prolonged course of neurosurgery after the acute infection. The 8-week-old infant (Case 1), the first to be treated with penicillin, was discharged with residual central nervous system damage and died when readmitted two months later, apparently because of this damage. Both the infants 3 and 4 months old (Cases 10 and 4, respectively) had fairly severe residual damage and were institutionalized. The 5-month-old infant (Case 3) who died had been sick for five days before admission and had been treated in another hospital with sulfadiazine. He developed a terminal complicating typhimurium bacteriemia and intestinal infection. The youngest living and apparently well infant (Case 14) was 3½ months old. This infant was the last one treated in 1944, and illustrates some of the conclusions drawn about therapy, based on our preceding experience. These will be mentioned in the subsequent discussion. The next youngest to make a good recovery was 5 months old and was treated almost entirely with penicillin (Case 6). The 8-month-old infant (Case 2) made a good recovery and had only transient residual paresis of one hand. Except for a single dose of sodium sulfadiazine, she received only penicillin. The 11-month-old infant (Case 9), who died within twenty-four hours of hospitalization, and the 13-month-old infant (Case 5), who died, had each been sick for two weeks before admission. The first of these had x-ray evidence of prolonged increase in intracranial pressure, and a pneumoencephalogram of the second infant indicated considerable loss of brain substance.

DISCUSSION

A few main features stand out in the analysis of the foregoing material and warrant a brief discussion. The figures show that since penicillin became available there has been a significant reduction in the mortality rate from pneumococcus meningitis in infants and children. The importance of this fact, however, is overshadowed by the realization that the percentage of surviving infants who will be competent members of society is still very low. It is for this reason that we are particularly interested in improving therapy for the patients under 2 years of age.

The therapy in the cases analyzed was directed toward: (a) sterilization of the blood and spinal fluid, and (b) prevention of adhesions and subsequent hydrocephalus and permanent brain damage. Unquestionably penicillin is an effective bactericidal agent against pneumococci when mixed with infected blood or spinal fluid. The only cases in which the spinal fluid was not permanently sterilized were those in which the history and spinal fluid findings suggested an infection of sufficient duration to allow the formation of walled-off pockets of pus. Even when the meningeal infection was of short duration, great difficulties arose when, because of its severity (as indicated by the large number of cells and pneumococci present), adhesions formed which were sufficient to block the circulation of cerebrospinal fluid. It was in the hope of reducing this latter hazard that, when feasible, fairly large amounts of infected spinal fluid were drawn off and replaced by oxygen and penicillin. However, when one considers the narrowness of the subarachnoid space in young infants, it is evident that even small fibrous strands can traverse and block the channels, thereby limiting the amount of fluid that can be drawn off or subsequently injected. Experience gained from treating patients in this way indicated that, even though the production of fresh spinal fluid might be promoted, the procedure did not guarantee against formidable adhesions.

The fact that the therapy was not uniform in each case is largely accounted for by the circumstances under which any new therapeutic agent is given clinical trial. In brief, the attempt was made to determine whether penicillin was more effective alone or in conjunction with other forms of specific therapy. In eight of the fourteen cases the spinal fluid was permanently sterilized within the first day of intrathecal therapy. Of four resistant cases (Cases 1, 3, 5, and 8), three proved fatal. In two of these (Cases 1 and 5) there were sterile spinal fluid cultures within two days after instituting penicillin therapy (although positive cultures were obtained at autopsy in Case 5). In the third there were recurrent positive cultures (Case 3). In the fourth case (Case 8) there was excessively purulent spinal fluid which was sterilized in three days, but the patient developed hydrocephalus. The remaining two were unfavorable cases from the point of view of duration of illness and both patients died within twenty-four to thirty-six hours of admission (Cases 9 and 13). Four of the above eight patients lived, with residua: two were only 6 weeks old (Cases 7 and 11), one of whom had been sick five days. The other had previously suffered neonatal cerebral damage. The third (Case 10) had been sick for one week,

and in the fourth (Case 4) an adequate explanation was not found for his failure to recover completely, except for the fact that early in the course of therapy great difficulty was found in releasing spinal fluid by lumbar puncture. The four remaining patients who recovered were more favorable from the point of view of age and duration of illness, with the exception of one (Case 4) just mentioned (Fig. 2).

It is interesting that in two of the cases with a good recovery (Cases 2 and 6), sulfadiazine was not used in conjunction with penicillin during the treatment except for one or two doses given before penicillin was started. In Case 6 there had been treatment with sulfamerazine elsewhere, but the blood culture was positive on admission here. Of the other two complete recoveries, Case 12 was a favorable case detected and treated early with sulfadiazine and penicillin. One patient (Case 14) was quite young (3½ months), had been sick four days or less, and was treated with sulfadiazine and penicillin.

If it is assumed that adequate doses of intramuscular and intrathecal penicillin can sterilize the circulating blood stream and spinal fluid, respectively, one must conclude that a failure of this sterilization to occur promptly is due to a focus of infection not adequately reached by the drug. The promotion of fibrin formation is a characteristic of the pneumococcus, and it is not difficult to visualize such a focus being formed by a fibrin "pocket," which, depending on its age, may be amenable to the medical therapy outlined, or only to a surgical or other mechanical approach for drainage and subsequent sterilization. Only early and vigorous treatment can prevent the formation of the thick plastic exudate that is seen at autopsy in the unfavorable cases. It is probably safer at present to use an appropriate sulfonamide in conjunction with penicillin until the need for this combination has been either more clearly established or disproved.

SUMMARY AND CONCLUSIONS

In summary, it may be said that this series of infants illustrates the favorable results which the addition of penicillin to the therapy of pneumococcus meningitis has achieved. Recoveries, either intact or with residual damage to the brain, were significantly more frequent than with sulfonamides and type-specific antiserum. Of fourteen infants, nine survived. However, five of these nine exhibited varying degrees of permanent central nervous system damage. They, with those who died, constitute the problem still confronting us.

In general, one may conclude that:

1. The younger the infant and the longer the duration of the infection, the poorer the prognosis. (Four of the fourteen patients whose cases are presented were under 2 months of age; two of the deaths were in older infants sick two weeks before therapy.)

2. Adequate penicillin therapy can sterilize the cerebrospinal fluid and blood stream within twenty-four hours if it is administered before heavy fibrinous exudate is formed in the meninges.

3. Penicillin therapy should probably be continued about one week after

sterilization of the spinal fluid, and sulfonamide therapy for a week or more longer if extrameningeal foci of infection are present or suspected.

4. In the presence of heavily infected spinal fluid, spinal drainage and replacement therapy with penicillin and oxygen, and possibly other special procedures, may be advisable. These measures await further clinical trial.

5. The value of type-specific antiserum, in conjunction with penicillin and an appropriate sulfonamide, such as sulfadiazine, has not as yet been sufficiently appraised.

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THE PREVENTION OF RHEUMATIC RECURRENCES IN CHILDREN BY THE USE OF SULFATHIAZOLE AND SULFADIAZINE

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THE daily administration of small doses of sulfonamides has been effective in reducing the incidence of streptococcal infections and recurrences of rheumatic fever. Sulfanilamide has been the drug employed in groups of children[1-10] and sulfadiazine has been employed for the reduction of streptococcal infections in large groups of the Armed Forces.[11, 12] No reports have appeared as yet which describe the use of any of the newer drugs in children. For two years we have employed sulfathiazole or sulfadiazine in groups of rheumatic children and are reporting here our experience with the effectiveness and reactions with these types of medication.

PROCEDURE

During the first winter season, 1943-1944, the treatment was given to twenty-two children residing in a convalescent home. Sulfathiazole was used exclusively in daily doses of 1 Gm. One tablet of 0.5 Gm. was given in the morning and another in the evening before meals. The treatment was started in early October and continued until the middle of May. During the first month of therapy, urinalyses, hemoglobin determinations, and leucocyte counts were performed at weekly intervals and thereafter once a month unless the patient's condition warranted more frequent tests. Erythrocytic sedimentation rates were determined frequently to detect incipient infection.

The following year, 1944-1945, the treatment was repeated and new patients added to the group. At the same time a prophylactic course of therapy was instituted at a school for handicapped children, employing sulfadiazine in daily doses of 0.5 Gm. The drug was administered as a single dose to each child upon arrival at the school in the morning. The same routine tests were performed for the detection of untoward reactions.

Whenever the condition of a child in either group improved so that he could be discharged from the respective institution, he was referred to a children's cardiac clinic where the prophylactic treatment was continued. Several other patients were added to the outpatient group to be treated throughout the winter season.

A total number of seventy children received prophylactic treatment for eighty-one patient seasons. There were fifty-nine children less than 14 years of age and eleven whose ages ranged from fourteen to seventeen years. Rheumatic attacks had occurred within the previous year in forty-five instances and at longer intervals in the remaining twenty-five. Seven children had had chorea as the only manifestation of the rheumatic syndrome. (Table I.) It was the policy to wait at least one month after all signs of rheumatic infection had dis-

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TABLE I. CHILDREN TREATED WITH SULFATHIAZOLE OR SULFADIAZINE

	AGE (YR.)	PATIENTS (NO.)	PATIENT SEASONS	SULFATHIAZOLE	SULFADIAZINE	RECURRENCES
Rheumatic Attack Within Previous Year						
	3 to 13	41*	50	42	8	0
	14 to 17	4	4	0	4	0
Rheumatic Attack More Than One Year Previously						
	3 to 13	18†	20	9	11	0
	14 to 17	7	7	2	5	0
Total		70	81	53	28	0
Treated less than 3 months		8	9	5	4	
Total		78	90	58	32	

*6 had chorea only.
†1 had chorea only.

appeared, including the return of the erythrocytic sedimentation rate to normal levels, before the prophylactic treatment was started. Some of the children had no evidence of valvular damage while others had far advanced mitral stenosis or combined aortic and mitral valvulitis.

Nine other children were treated for only one or two months. Four were uncooperative, four developed such severe albuminuria that the treatment was terminated, and the remaining one had been treated only two months at the time of this report.

RECURRENCES

None of the children developed recurrences of rheumatic symptoms while under treatment. One child, who entered the convalescent home too late in the first winter season to be included in the group, developed an attack of polyarthritis and an exacerbation of cardiac symptoms. Included in the series the following year he spent an uneventful winter. One child developed an exacerbation of rheumatic fever in the late summer about three months after her first course of prophylactic treatment had terminated.

Two other children developed subacute bacterial endocarditis with blood cultures repeatedly positive for streptococcus viridans. In one patient, severe manifestations of the illness started at the end of the summer, about three months after termination of the first winter's course of drug had been completed. The other child developed very mild symptoms, consisting chiefly of loss of weight, which were first noted about one month after the course of sulfadiazine had been instituted. Following intensive courses of penicillin therapy, both patients recovered and have remained free for a period of nine and six months, respectively.

The amount of drug in the circulating blood was measured only occasionally. Generally the levels were slightly more or less than 1.0 mg. per cent. In only two instances was it above 3.0 mg. per cent; in one patient receiving 1 Gm. of sulfathiazole daily it rose to 5.1 mg. per cent and in one receiving 0.5 Gm. of sulfadiazine it reached 3.8 mg. per cent. In three children attending the outpatient clinic, no amount could be detected at times in the blood serum, suggesting that these patients were not taking the drug at home as faithfully as they claimed.

TOXIC REACTIONS

Albuminuria without other evidence of nephritis was the most frequent reaction encountered and it occurred exclusively in the group of children receiving sulfadiazine. Traces of albumin in the urine were not considered abnormal but there were five children who had larger amounts appearing at various periods ranging from three weeks to five months after the treatment was instituted. In several instances the drug was discontinued for a few days until the urine cleared, but all continued their courses of treatment throughout the season. Four additional children had such large amounts of albumin in their urine that the drug was withdrawn permanently from three to five weeks after initiation of the course. One of these patients had had a course of sulfathiazole the preceding year without urinary symptoms. None of the four patients had any subjective symptoms, any blood or casts in their urine, hypertension, or elevated blood urea levels. Subsequent tests have indicated that orthostatic conditions may have influenced the degree of albuminuria in at least three of these patients. Two other children with albuminuria before treatment was started continued the course without exacerbation of symptoms.

Leucopenia occurred in two children receiving sulfathiazole and in two receiving sulfadiazine. The white blood cells ranged between 3,000 and 4,000 per cubic millimeter on occasions and returned quickly to normal when the drug was withdrawn for a week. In each case, the white blood cells remained at satisfactory levels after the drug had been started again.

Mild erythematous rashes occurred in two patients, but it was questionable whether they were directly caused by the drug, and they disappeared within a few days without withdrawing the drug.

Other reactions such as nausea, vomiting, and fever were not noted in either series of patients (Table II).

TABLE II. TOXIC REACTIONS

	PATIENT SEASONS	NUMBER REACTIONS	PER CENT	DRUG WITHDRAWN	PER CENT	TYPE OF REACTION	TIME OF OCCURRENCE
Sulfathiazole	58	3	5.2	0	0	2 leucopenia; W.B.C. between 3,000 and 4,000	Fifth to seventh month
						1 rash	6 weeks
Sulfadiazine	32	12	37.5	4	12.5	4 severe albuminuria	1 to 3 weeks
						5 mild albuminuria	3 to 20 weeks
						2 leucopenia; W.B.C. between 3,000 and 4,000	12 weeks
						1 rash, mild	2 weeks

The difference in incidence of toxic reactions among the two groups may have arisen from the choice of patients in each group. Statistical analysis showed that such a difference in the number of reactions and the number of patients withdrawn from the group could not have arisen from chance alone (Chi square values were 13.3 and 4.9, respectively, with corresponding values of P of 0.0003 and 0.026).

COMPARISON OF THE INCIDENCE OF REACTIONS

It is rather difficult to compare the incidence of toxic reactions reported by different authors, because of various criteria employed in judging toxicity. In the groups of children treated with sulfanilamide the incidence of all forms of reactions based upon patient seasons varied from 10.6 to 37.0 per cent. Probably a more accurate method is the comparison of percentages of children withdrawn from the groups because of severe reactions, a method employed by Dodge and associates[9] in their report. Such percentages varied from 0 to 37.0 (Table III). These wide differences may be explained in part by the various ways the authors managed their toxic patients. Some immediately discontinued the prophylactic therapy, while others stopped treatment or reduced the dose for a short time and then resumed the regular course with the patient under observation. It was felt that nothing would be gained by adding the total number of patient seasons and reactions of the previous reports to provide comparison of the incidence of toxic reactions with those of our own series.

TABLE III. TOXIC REACTIONS REPORTED BY OTHERS

AUTHOR	PATIENT SEASONS	NUMBER REACTIONS	PER CENT	DRUG DISCONTINUED	PER CENT	TYPE OF REACTION
			Sulfanilamide			
1. Coburn and Moore[1]	85	--	--	5	5.8	
2. Hansen and associates[4]	78	10	12.8	1	1.3	1 leucopenia; W.B.C. below 2,000 9 rash, nausea, vomiting
3. Kuttner and Reyersbach[5]	108	15	13.9	15	13.9	3 leucopenia; W.B.C. below 3,000 12 fever, rash, nausea, vomiting
4. Chandler and Taussig[7]	47	5	10.6	5	10.6	2 leucopenia; W.B.C. below 3,500 3 rash, jaundice
5. Feldt[8]	107	22	20.6	4	3.7	10 leucopenia; W.B.C. below 4,500 12 rash, nausea, vomiting
6. Stowell and Button[10]	46	17	37.0	17	37.0	9 rash, nausea, vomiting 7 leucopenia 1 agranulocytosis and death
7. Dodge and associates[9]	181	41	22.7	0	0	41 leucopenia; W.B.C. below 5,000
			Sulfadiazine			
Present series	32	12	37.5	4	12.5	2 leucopenia 9 albuminuria 1 rash
			Sulfathiazole			
Present series	58	3	5.2	0	0	2 leucopenia 1 rash

There have been no reports of the use of sulfathiazole and sulfadiazine except those of Hansen and associates[4] and Kuttner and Reyersbach[5] who employed this drug in a few cases when sulfanilamide was not tolerated. Hansen and associates observed one case of leucopenia of 1,700 white cells per cubic centimeter following sulfathiazole therapy. Kuttner and Reyersbach gave sulfadiazine to five children and one of these developed symptoms of fever and abdominal pain.

The reports[11, 12] from army camps where sulfadiazine was administered to large groups of men mention reactions consisting chiefly of dermatitis and granulocytopenia. One severe case of hemolytic anemia occurred but the percentage of men with severe symptoms was small.

SUMMARY AND CONCLUSIONS

A group of seventy children receiving sulfathiazole or sulfadiazine for a total of eighty-one patient seasons suffered no recurrences of rheumatic fever during the periods of treatment.

One child developed a recurrence during a summer season between courses and another developed subacute bacterial endocarditis during the same period. A third child developed subacute bacterial endocarditis while being treated.

Reactions among seventy-eight children treated for ninety patient seasons, consisted of albuminuria in nine patients receiving sulfadiazine, and in four instances it was so severe that the drug was withdrawn. Mild leucopenia occurred in four patients, two of whom were receiving sulfadiazine and two sulfathiazole, but the number of white cells quickly returned to normal when the drug was withdrawn for a few days. Slight rashes occurred in two children but none of the group developed symptoms of nausea, vomiting, or fever.

Although the reactions were mild, they sometimes occurred as late as five months after the inauguration of the course of treatment.

Sulfathiazole and sulfadiazine appear to be safe and effective drugs to administer prophylactically to children over long periods of time, but the patients must be observed frequently for the detection of reactions. It must be certain that the patient has completely recovered from his acute infection before prophylactic treatment is started.

Since rheumatic infections occur during the summer months, it seems likely that the prophylactic treatment with sulfonamides should be continued throughout the entire year. In many cases it would seem advisable to administer the drug continuously for several years.

The hospital, school, and convalescent home seem better places to administer the treatment than the office or outpatient clinic because of the opportunities to observe the patients closely and to be certain that the drug is taken regularly. However, if the patient is cooperative and if laboratory facilities are available to the physician in his office or clinic, it is practical to treat the child as an outpatient and thus shorten the period of his stay in the hospital or convalescent home.

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RICKETS: A STUDY OF CALCIUM AND PHOSPHORUS METABOLISM AND OF CLINICAL FINDINGS AS INFLUENCED BY CERTAIN FEEDINGS

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THIS report is a summary of a study of calcium and phosphorus metabolism as influenced by different carbohydrates in the diet. It originated in an effort to correlate the following three apparently unrelated observations.

1. In spite of supposedly adequate dosage of vitamin D many babies develop mild clinical rickets.

2. Bergeim,[1] in 1926, reported that the addition of lactose to the diet of albino rats led to improved absorptions of calcium and phosphorus by increasing the acidity of the intestinal contents. He thus offered an explanation for the findings of the numerous observers[2] who have suspected some relationship between lactose in the diet and calcium and phosphorus metabolism.

3. In 1933, one of us[3] found that lactose when added to feedings of diluted cow's milk led to a stool more acid than did maltose-dextrin.

The tripod of these findings became the foundation of the following questions and studies.

1. Do maltose-dextrin preparations by decreasing the acidity of the stools interfere with the optimum absorption and retention of calcium and phosphorus and thus necessitate greater therapeutic doses of vitamin D? A comparison of the retentions of calcium and phosphorus on formulas containing maltose-dextrin with those containing lactose should be of interest and is the real basis of this study.

2. Are the retentions of calcium and phosphorus related to the pH of the stool?

3. Is there correlation between the type of carbohydrate in the formula, the pH of the stool, and the fecal flora?[4]

4. Are there any demonstrable clinical differences between infants receiving lactose in their formulas and those receiving maltose-dextrin?

LITERATURE

Space prevents any attempt at reviewing the enormous literature on calcium and phosphorus metabolism, and on vitamin D. The reader is referred

From the Sarah Morris Hospital for Children and the Nelson Morris Institute for Scientific Research of the Michael Reese Hospital. Financed in part by Mead Johnson and Company and in part by the Otto Baer Fund for Clinical Research of the Michael Reese Hospital.

The chemical study was under the direction of Dr. David J. Cohn with the technical assistance of Miss Grace Lawrence.

The publication of this report, presented before the Michael Reese Hospital Session of the American Academy of Pediatrics in Chicago, 1942, has been withheld until the completion of the study of breast-fed infants during the winter season. Reports of progress have previously been given at the scientific exhibit of the American Medical Association (Kansas City, Mo., May 11 to 15, 1936), at the Chicago Pediatrics Society, Dec. 18, 1934, and April 20, 1937, at the Chicago Society of Internal Medicine, March 22, 1937, and at the Michael Reese Hospital Session of the American Academy of Pediatrics (Chicago, Nov. 4, 1942). These have appeared in the Proceedings of the Institute of Medicine of Chicago **10**: 241, 1935; **11**: 313, 1937; and **11**: 329, 1937.

to the comprehensive treatise of Hess,[5] the monograph of Schmidt and Greenberg,[6] the excellent reviews of Kline, Keenan, Elvehjen and, Hart,[7] of Jeans,[8] Stearns,[9] the Council on Foods,[10] Leitch,[11] and many others for the literature of the last two decades. The number of recent contributions is overwhelming. However, most observers use a rachitogenic diet in their animal experiments. Many of the studies in human beings are on older children, while the studies on infants include the use of vitamin D in some form even in breast-fed infants.[12]

PLAN

In contrast to most of the work on calcium metabolism our study was unique in that none of the infants received any known forms of vitamin D during their stay in the hospital, and during the summer were never exposed to direct sunlight. We tried as far as possible to determine the effects of food per se. The technique of the metabolism experiments was the same as in previous communications.[13] Feedings consisted either of breast milk; undiluted cow's milk; undiluted cow's milk with the addition of 12 per cent lactose or maltose-dextrin (only two infants); or mixtures of undiluted cow's milk with 12 per cent lactose or maltose-dextrin and diluted with distilled water to one-half or in older infants to two-thirds strength. All cow's milk was boiled one minute. Some babies received the lactose, others the maltose-dextrin mixtures during the entire period. Some were started on one sugar and changed to the other.

Metabolism periods lasted forty-eight hours and averaged one or two periods per week. The fact that each infant was observed and studied over a period of six months explains the length of time spent in arriving at any conclusions.

Determinations of calcium and phosphorus were made in aliquot specimens of the daily pooled food, stools, and urine.

The study included monthly determinations of blood calcium and phosphorus as well as semimonthly x-ray examinations of the long bones and ribs.

Physical examinations were made daily.

During the last twelve years we have studied over forty infants during their first six months of life. The innumerable annoyances and mishaps familiar to those who have conducted metabolism experiments ruined many observations, but we have been able to conduct satisfactory studies of calcium and phosphorus balance in fifteen babies. The prolonged period of observation in each case obviated the complicating question of tissue depletion raised by some writers.[14]

RESULTS

Our results are summarized in Chart A and Charts 1 to 4 which are typical of the entire study. The average retentions of calcium and phosphorus for each period per kilogram body weight per day are indicated in the vertical blocks. The heavy black line above is the weight curve. The broken lines immediately below the weight curve represent the rate of calcium and phosphorus retention. In Chart A (the normal breast-fed infant) these broken lines have been arbitrarily adjusted so as to parallel the weight curve. On all the other charts the ordinates are the same as in control Chart A. Thus, inclination toward the weight curve shows higher retention than the average of human milk feedings.

Inclination down and away from the weight curve shows either less retention or loss.

To conserve space we are not submitting the numerous tables of analyses. Charts A and 1 (*a*) and (*b*) show the findings in the breast-fed infant during different periods of the year. In all seasons the stools are highly acid with a pH of 4.5 to 5.0.

Chart A is typical of the breast-fed infant during the summer season and so serves as a control. The retentions of calcium and phosphorus like the weight curve proceed in regular orderly fashion, there being little variation from day to day. It should be noted as explained that in this instance the ordinates of the broken lines showing calcium and phosphorus retention have been arbitrarily adjusted so that they parallel approximately the weight curve.

CHART A. FEEDING: HUMAN MILK

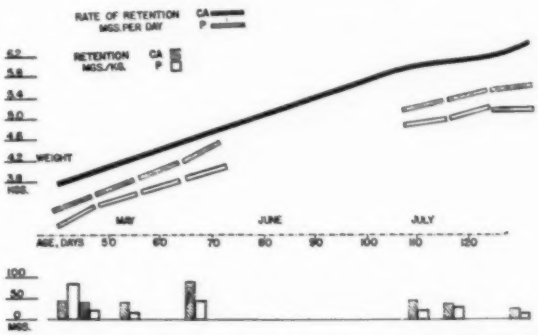

Chart A.—This chart should serve as a control. It shows the findings with feedings of breast milk during the summer. The retentions are uniform and regular.

Chart 1 (*a*) and (*b*) shows the results in breast-fed infants during the winter and spring. During the winter and spring seasons the curves of calcium retention are not as orderly as during the summer; still the retentions proceed in satisfactory fashion even though no appreciable amount of vitamin D can be found in human milk.[15]

It would seem probable that factors other than vitamin D alone may be important in preventing the development of rickets in babies under 6 months of age.

Chart 2 (*a*) is that of a baby receiving undiluted cow's milk during the winter. The findings are in sharp contrast to those of the breast-fed infant. The stools tend to complete alkalinity with a pH range over seven. The retentions are irregular, often broken by considerable loss of calcium. When retention occurs it is irregular in amount and in no way comparable to that of the breast-fed infant.

Chart 2 (*b*) shows the results in a baby receiving undiluted cow's milk during the summer. The stools remain alkaline. But mineral losses are changed

to hyper-retentions. Compared to the breast-fed infant in summer (A) the infant is hypermineralized. The retentions are highly satisfactory in amount but erratic. The rate of mineral retention can in no way be compared in smoothness to that in the breast-fed infant.

CHART 1. FEEDING: HUMAN MILK

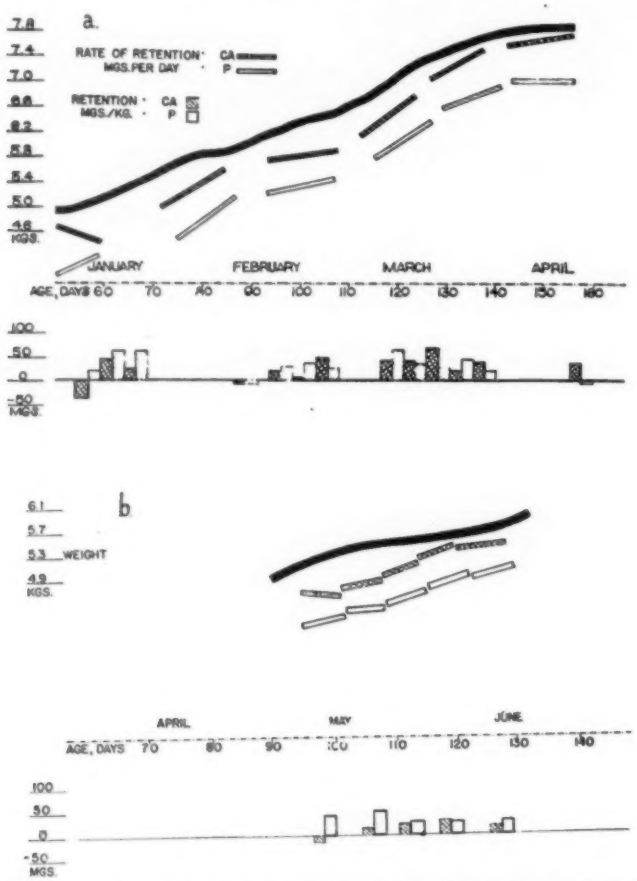

Chart 1 (*a*) and (*b*).—This chart shows the findings with feedings of breast milk during the winter (*a*) and spring (*b*). The retentions are not as uniform and orderly as during the summer but are quite satisfactory.

Chart 3 (*a*) and (*b*) is typical of the babies receiving dilutions of cow's milk with the addition of maltose-dextrin.

Chart 4 (*a*) and (*b*) shows the findings in babies receiving dilutions of cow's milk with the addition of lactose.

The findings in the babies receiving milk dilutions (Charts 3 and 4) are astonishing. The pH of the stools lies between that of the breast-fed and the

infant on undiluted cow's milk, with lactose leading to a slightly greater acidity than maltose-dextrin. But whether the formula contains lactose or maltose-dextrin the retentions are surprisingly good. And this during the winter season and in the absence of any known vitamin D! Surely, here is an observation

CHART 2. FEEDING: COW'S MILK

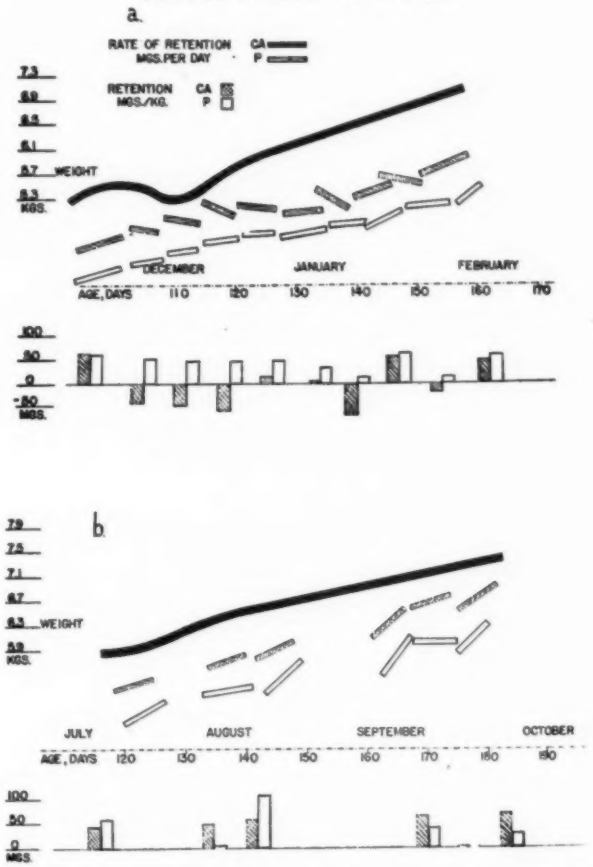

Chart 2 (*a*) and (*b*).—This chart shows the findings with feedings of boiled whole cow's milk during the winter (*a*) and summer (*b*). In winter the retentions of calcium are extremely irregular. Many losses are registered. Summer seems to produce hypermineralization.

that requires further study. It must be remembered, however, that this study was limited to babies under 6 months of age.

There seems also some relationship between the retentions and the weight curve. Down-grade curves are accompanied by poor mineral retentions or at times by actual losses.

Besides a comparison of the effects of lactose and maltose-dextrin our study questioned a possible correlation between calcium and phosphorus retention and

the pH of the stool. The pH of every stool during the metabolism periods was determined. On the diluted lactose mixtures the resulting pH of the stool never consistently reached and remained at that of the breast-fed infant (pH 4.5 to 5.0) though always more acid than the stool of the infant on maltose-dextrin feedings. This, of course, prevented a real comparison of the effect of stool acidity upon the mineral retentions.

CHART 3. FEEDING: MALTOSE-DEXTRIN

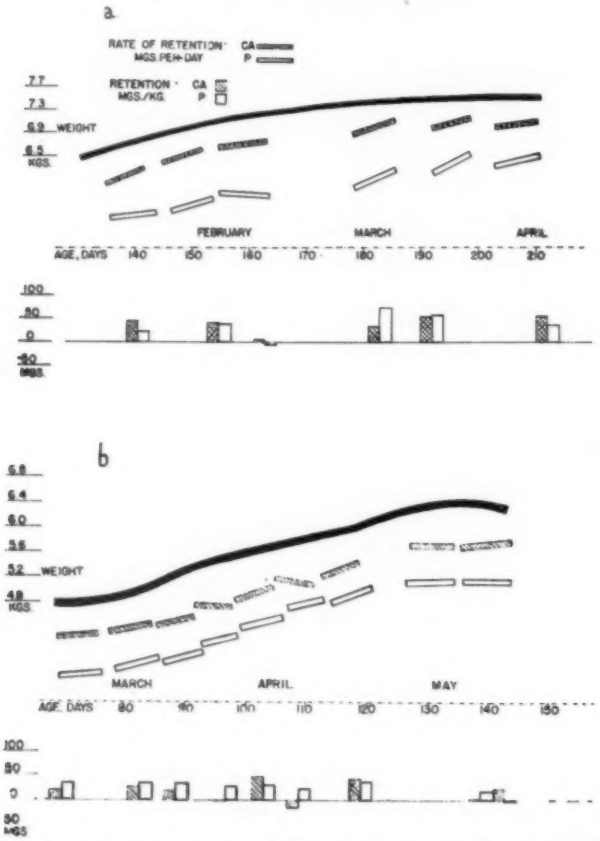

Chart 3 (*a*) and (*b*).—This chart shows the findings on feedings of diluted boiled cow's milk with maltose-dextrin during late winter (*a*) and spring (*b*). The retentions are unexpectedly good.

In no instance could we find any daily specific relationship between the pH of the stool and the amount of the retention of calcium and phosphorus.

Only in the general averages of all experiments over the entire period, leaving out, of course, the summer observations with the complicating ultraviolet, was there any such relationship indicated.

Table I shows these averages. This table summarizes the entire study. It shows: (a) On feedings of breast milk—almost equal retentions in milligrams per day of calcium and phosphorus both summer and winter. (b) On undiluted cow's milk—extreme variability, decided differences between retentions of calcium and phosphorus and extremely low retention of calcium during the

CHART 4. FEEDING: LACTOSE

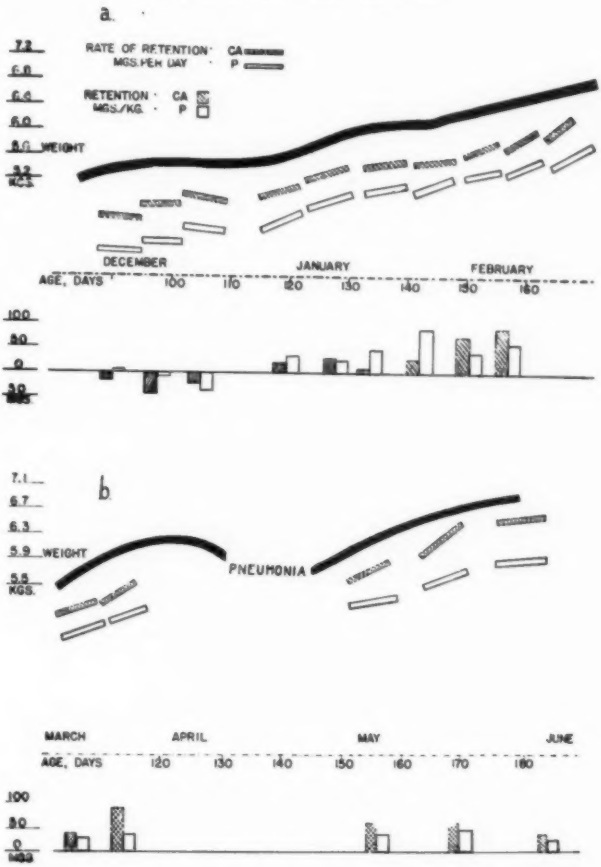

Chart 4 (*a*) and (*b*).—This chart shows the findings on feedings of diluted boiled cow's milk with lactose during winter (*a*) and spring (*b*). With the exception of three determinations during December the retentions are surprisingly good.

winter; and actual hypermineralization when compared to the breast-fed infant during the summer. (c) On milk dilutions with either lactose or maltose-dextrin—surprisingly good retentions on either feeding even during the winter. Those from lactose are slightly higher.

TABLE I*

FOOD	RETENTION IN MG. PER KG. BODY WEIGHT PER DAY		pH OF STOOL	
	CALCIUM	PHOSPHORUS	RANGE	MEAN
Breast milk (summer)	33.5	34.0	4.3-6.5	4.9
Breast milk (winter)	26.5	28.0	4.3-6.5	4.9
Undiluted cow's milk (winter)	1.0	35.4	5.0-8.5	7.4
Undiluted cow's milk (summer)	38.9	42.5	5.0-8.5	7.4
Diluted cow's milk with maltose-dextrin	24.9	17.2	4.4-8.5	7.0
Diluted cow's milk with lactose or beta-lactose	33.1	29.6	4.3-8.5	6.0

*This table shows the average retentions of calcium and phosphorus and the range and the mean of the pH's of the entire study.

CLINICAL OBSERVATIONS

The clinical conclusions corroborate those reported some years ago.[16] We found the rosary and Harrison's groove to be the most valuable signs in early diagnosis of rickets appearing months earlier than changes in blood calcium and phosphorus, or x-ray. Craniotabes proved unreliable, appearing at times about the third month and disappearing spontaneously toward the end of the fourth or in the fifth month.

On the different feedings the incidence of rickets was as follows:

A. Breast Milk

Five babies showed no clinical rickets.

B. Milk dilutions with carbohydrate

Ten babies showed practically no clinical rickets.

Fifteen babies showed a very slight rosary and Harrison's groove. These were no more marked than in many babies receiving supposedly adequate amounts of cod-liver oil and usually pronounced normal.

Five babies showed a definite rosary and Harrison's groove, but x-ray and blood chemistry findings were normal.

The babies on lactose seemed slightly superior with respect to tissue turgor, alertness, and general vitality. These findings are of course highly subjective but such disinterested observers as interns, and nurses came to the same conclusion.

C. Undiluted cow's milk with 12 per cent carbohydrate

The two babies on this feeding showed abnormally rapid rates of growth. Coincidentally they developed such marked clinical signs of rickets that the experiment was stopped and not repeated. No metabolism observations were possible in these two.

In addition to the factors of food and season we began to surmise that repeated common, ward infections may be more significant than usually suspected, or at any rate infections in connection with constitutional inferiority. The five babies on milk dilutions who developed clinical findings of rickets were of the debile type and each suffered from several attacks of coryza and bronchitis while in the ward. Observers have long noted the inter-relationship of rickets and infection. In our cases the infections seemed to precede the rachitic findings.

Recently Follis, Jackson, Eliot, and Park[17] in carefully conducted pathologic studies reported rachitic changes in older children dying of acute infections. We began to suspect that constitutional inferiority, presumably based on improper prenatal care, plus repeated infections may be a cause as well as a result of rickets.

Finally with respect to the weight curve, we had the impression that the more closely the curve approximates that which it would have been, had the baby been breast fed, the less likely is that baby to develop rickets.

DISCUSSION AND SUMMARY

Our original study was planned to compare and to correlate if possible the retention of calcium and phosphorus, the pH of the stool, and the clinical findings in babies receiving lactose with those receiving maltose-dextrin.

Our chemical studies showed that the stools of babies on lactose were on the average more acid than those on maltose-dextrin and that the calcium and phosphorus retentions were slightly higher in the former. But the differences were not highly significant and in no specific case could the retention be definitely related to the pH of the specific stool. A far greater influence on the retention of calcium and phosphorus was the effect of season. The retentions in the summer were far the greatest.

Diet does play some role, however, as is shown by comparing the results obtained in the feedings of breast milk with those of cow's milk. Babies receiving breast milk with no vitamin D of any sort showed uniform orderly retentions during the summer, and almost as satisfactory retentions during the winter despite the low vitamin D content.[15] Babies on undiluted cow's milk in winter showed retentions or losses that were irregular and disorderly and in summer showed irregular retentions and often hypermineralization compared to the breast-fed infants. These findings, especially those of the winter season, become all the more important when we realize that breast milk contains about one-sixth as much calcium and phosphorus as does cow's milk. (Breast milk per liter: calcium monoxide, 0.3 to 0.4 Gm.; phosphorus pentoxide, 0.24 to 0.4. Cow's milk: calcium monoxide, 1.7 to 2.0; phosphorus pentoxide, 2.0 to 2.4.)

Unfortunately the onset of the war prevented an elaboration of these studies. It would have been most interesting to experiment with other combinations of milk and lactose to see if we could find a combination that would maintain the stool at a pH of from 4.5 to 5.0. It also would have been interesting to try the effect of a low percentage of carbohydrate added to undiluted cow's milk.

Clinically the findings paralleled the chemical. Babies on breast milk averaged the best. Very close to them, however, were the babies receiving milk dilutions with the addition of carbohydrate, those on lactose being possibly slightly superior to those on maltose-dextrin. Babies on undiluted cow's milk developed signs of rickets during the winter in spite of their slower rate of growth but made perfect clinical recoveries during the summer. Only the chemical determinations showed any abnormality during the summer. Babies on undiluted cow's milk with 12 per cent carbohydrate, either lactose or maltose-dextrin, gained very rapidly and developed marked signs of rickets.

In other words, in babies under 6 months, independent of the influence of vitamin D, human milk is not rachitogenic. Undiluted cow's milk seems rachitogenic, certainly during the winter. Usual dilutions of cow's milk with carbohydrate addition do not, as a rule, seem rachitogenic in babies under 6 months of age even during the winter but become so when either the concentration of the milk, the amount of carbohydrate, or both lead to a gain in weight more rapid than would have resulted from breast milk feeding.

Possibly intercurrent infections play a role, particularly in debile infants. They may enhance the rachitogenic influence of improper mixtures, while the summer season with its ultraviolet light is powerfully curative.

Perhaps the entire clinical study can be summarized in emphasizing the importance of the weight curve. This is, after all, a composite of feeding, season, infection, constitution, and care. The closer it parallels the curve that could be expected if that same baby had been breast fed, the less likely is that baby to develop clinical rickets; the more it deviates upward the more likely is the baby to become rachitic. When it deviates downward, rickets is slower to develop, but on feedings of undiluted cow's milk in winter, at any rate, the baby will eventually show signs of rickets.

It must be remembered that this study is of the influence of certain dietetic components upon calcium and phosphorus metabolism, independent of the effect of vitamin D. It does not in any way cast doubt upon the effect and value of vitamin D in facilitating calcium and phosphorus retention.

Summarizing the chemical and clinical study as a whole, it would seem from the standpoint of calcium and phosphorus retentions and clinical observations that breast milk remains the ideal food, and dilutions of cow's milk with carbohydrate addition, a very close second. The type of carbohydrate used is inconsequential compared to the importance of milk dilution. Of carbohydrates studies lactose is perhaps superior. Whole cow's milk proved undesirable, and whole cow's milk with high carbohydrate seems to be actually injurious.

As early as 1917 one of us[18] on the basis of clinical experience and European teachings recommended the use of milk dilutions with carbohydrate addition and again in 1932 in a critique of lactic-acid milk[19] raised the question as to whether this mixture with carbohydrate addition does not lead to overfeeding.

These studies force the question as to the advisability of many of the formulas and methods of feeding now so popular. Unquestionably the use of feedings of undiluted or slightly diluted cow's milk with too much carbohydrate or the early use of cereal lead to rapid gains in weight and to big babies. But are we not too ambitious in our efforts to improve upon nature? Perhaps the very composition of our feedings is in itself necessitating the constantly increasing dosages of vitamin D that we prescribe; and even leading to mild rickets in babies receiving supposedly adequate dosage of this vitamin. Perhaps we should revert to our former masters a bit and pay more attention to the regulation of the calorie value of our feedings. Perhaps, after all, the American slogan "Bigger and Better" should not be applied too rigorously to babies.

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PROCTOLOGICAL PROBLEMS OF THE PEDIATRICIAN

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THE pediatrician is consulted in many problems of infancy and childhood which on investigation prove to be proctological in origin.

The embryology and juvenile anatomy of the anorectal region must be recalled for complete understanding of these disturbances of its function. The lower pouching end of the hind gut, a closed blind-ended tube forms the rectum. The anus is constituted by an external dimple which deepens upward to become the so-called proctodeum. If these processes fail to approximate each other, we have the major defect of an imperforate anus to deal with, but normally a junction takes place, the continuity of the resulting tube being blocked on first contact by only the entodermal mucosa of the rectum and the ectodermal skin of the rectal dimple. The mesodermal sphincter muscle has formed around this junction and if evolution proceeds properly, the interposing skin and mucosa dissolve away completely leaving at their periphery a somewhat serrated mucocutaneous union called the dentate or pectinate line, which at birth, when unpuckered, by relaxation of the phincter has a diameter of a half inch or so. The fetal rectum and sigmoid colon are made generously as to length, and loop up into the pelvis much higher and more tortuously than later in life. As a consequence of this relative redundancy there are more turns and twists for gas and stool to negotiate just before evacuation in infancy than later on. Furthermore the infant sacrum is less hollow and more vertical than later, and the rectum is often less securely attached to it.

Constipation manifested by deficient, difficult, or painful movements of gaseous or material bowel contents, or by abnormal stool, is the most common complaint which, after elimination of other causes, leads to the rectum as the focus of disorder.

One of the fairly frequent sources of such trouble in the very young is an incomplete dissolution of the membranes intervening between the hind gut and the proctodeum. This failure may be of any degree from complete, to slight, and gives trouble proportionately. Undoubtedly a great percentage of babies are born with some vestige of this fetal diaphragm persisting and blocking or encircling the rectum, but in most it is evidently thin and tenuous enough so that the baby can complete its disposal by forcing a good-sized stool through it, for once it is broken up, it never re-forms or cicatrizes and gives no further trouble. But in many other cases it is too extensive or tough for the act of evacuation to do away with it, and in these cases the baby needs help. This need for help may be evidenced in several different ways. The baby may strain hard, puff and pant and groan, and after prodigious effort produce a small, ribbon or pencil stool. Or the baby may balloon up with gas which he

cannot pass without repeated suppositories, rectal tubes, enemas, stupes, or all of these. Or there may be fresh blood on the stool. These difficulties may be manifested at birth, but may not develop to a critical degree for days or even weeks. The reason for this delay can be that the opening, though small, may be adequate at first, but as time goes on, the effort at each stool keeps jamming the puckered-up mucosa of the segment of rectum immediately above the constriction down into the funnel above the anus, piling the folds of mucosa up on each other, causing them to overlap across the lumen, thus forming a very efficient valve. The more force exerted from above against the stool or gas the baby wishes to pass, the tighter these valves are closed. With repetition of this bruising pressure, congestion, then edema develop in the mucosal folds, magnifying the trouble and sometimes even producing free bleeding.

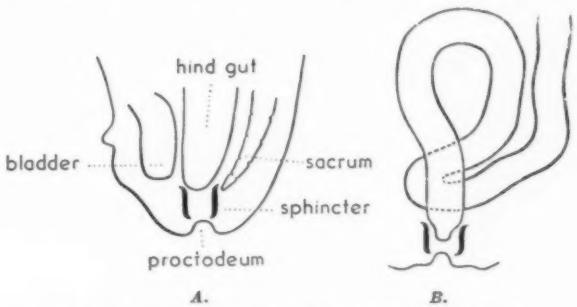


Fig. 1.—*A*, embryo (side view). *B*, infant sigmoid.

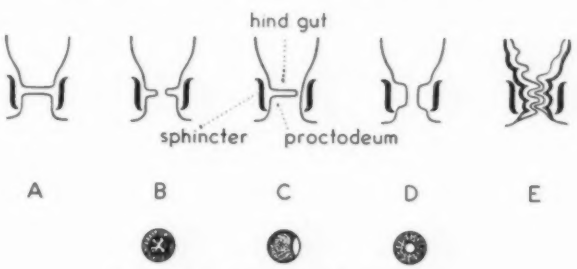
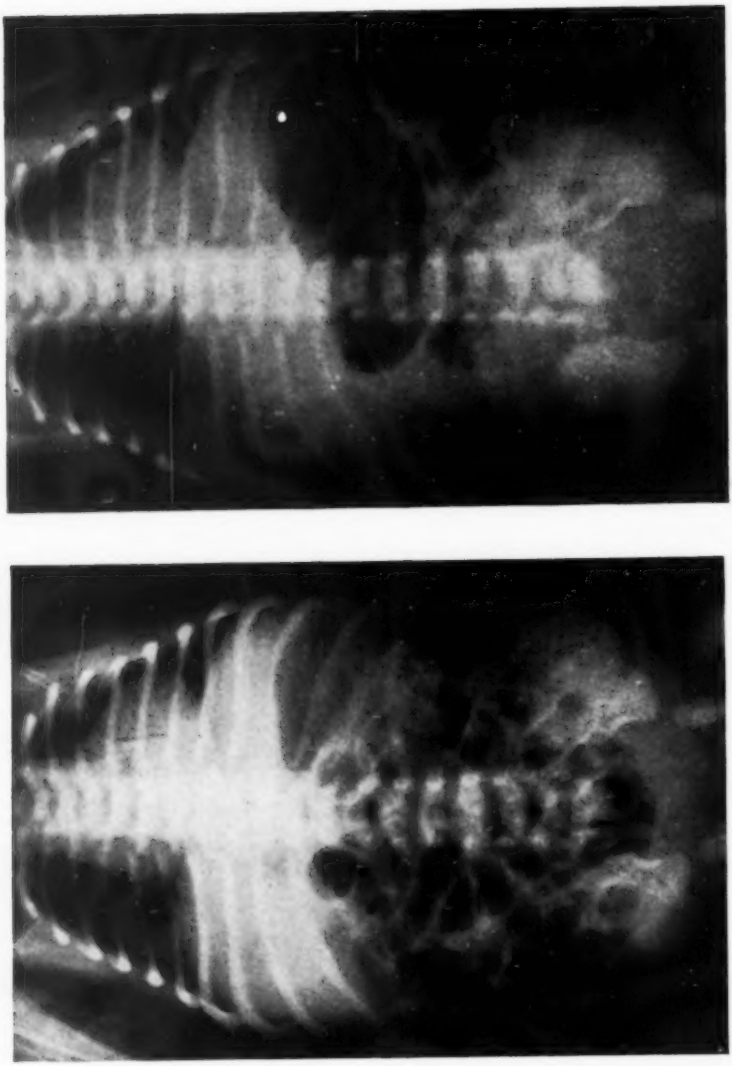


Fig. 2.—Varieties of rectal obstruction.

The best way to find out if rectal constriction is responsible is with a rubber covered finger, which the average newborn rectum should admit to the second joint without undue stretching.

In making the examination, and in dilating the stricture if present, the lubricated finger tip need only be placed against the anus, and the baby will do the rest. Force is not necessary and indeed is contraindicated. If there is a partial diaphragm present its edge can usually be felt or at least something can be felt to give away before the advancing finger tip; and if there is a ring of undissolved tissue—as is the most frequent condition—it is felt to en-



B.

A.

Fig. 3.—Case 1. *A*, twenty-four hours before rectal dilation. *B*, twenty-four hours after rectal dilation.

circle the finger tip and bind it like a ring of wire. Continued gentle pressure of the tapering finger causes the baby to bear down and accomplishes its own dilation. This may be done completely at once if the band is not too rigid. More marked degrees, however, may require several treatments at suitable intervals, because even the mildest stretching produces some degree of shock to the baby, and after a fairly forceful dilation the baby may lie very quietly and exhibit a dusky pallor for many minutes. When dilation is adequate, the mucosal folds find room to fall away from each other, allowing fecal matter and gas to pass freely as intended. Since the abnormal diaphragm or ring is bloodless in most cases, full dilation may be accomplished without bleeding, but occasionally one or a few subsequent stools may be bloodstained.

CASE REPORTS

CASE 1.—Baby with increasing abdominal distention, colic, and constipation beginning at birth. On the third day of life a flat abdominal x-ray was ordered by the delivering doctor because a serious obstruction was suspected. It showed the entire intestinal tract full of gas. The exploring finger encountered a wire-band-like ring stenosing the rectum. A single dilation accomplished complete deflation and relief. X-ray subsequently showed only a normal amount of gas.

CASE 2.—Baby seen first at 1 month of age because of colic, continued effort to move bowels, frequent, small vermicular stools a quarter of an inch in diameter. Rectum would not admit a finger tip but took a thermometer. Dilation started with a small otoscope speculum. Repeated daily at first, then gradually less frequently, until completely dilated at about 3 months of age. The mother was trained to do the later dilations.

CASE 3.—A 2-week-old baby who had had frequent loose stools since birth, the last two days mixed with considerable fresh frank blood. There was too much blood present to make a good proctoscopic examination without preparatory flushing so a finger exploration was done, revealing a wire-band-like stenosis of the rectum. After a single dilation bleeding diminished at once and stopped overnight.

Another rectal problem is painful defecation, sometimes so marked as to bring about voluntary retention, with consequent severe constipation. The mother reports that the baby cries piteously with each movement, or that the older child holds in, and seems to dread defecation and gives evidences of tenesmus and pain at stool. The usual cause is found on examination to be a fissure, or an area of proctitis. The situation develops into a vicious cycle because voluntary retention results in a larger, drier, harder stool, which abrades or lacerates the already injured mucosa or mucocutaneous area still more than it already is injured, and undoes any healing that may have taken place. In turn this additional trauma increases pain, adds to the retention, and results again in large, hard stool masses.

External fissures are readily visible on inspection if the sphincter is pulled partly open by the gloved fingers. Internal lacerations or areas of proctitis can be seen only with a proctoscope. In an infant or small child no better proctoscope can be desired than an electric otoscope, using a large speculum. If the outside of the tip is lubricated, with the child held firmly in the lithotomy position, insertion of the conical speculum is easy. The speculum can be used for applications of a topical nature. Child-sized proctoscopes are on the market

for those who prefer them. It may be necessary to flush the rectum out clean a little while before examination, to keep stool from coming down into the field of inspection, but usually this is not necessary.

Proctitis is seen as a cherry red congested field of mucosa contrasting with the pale pink normal tissue around it. Fissures are usually produced by a sharp or jagged protuberance on the stool. A fiber or hair may cut as it passes lengthwise. Proctitis is usually produced similarly, but may be started by an attack of diarrhea. Once injured the denuded mucosa or integument is subject to some degree of secondary infection. Before healing can take place another stool comes along, splits the fissure or stretches the area of proctitis and scrapes off any protective exudate or new cells, and the infection also retards healing.

For proctitis or fissure to heal, the stool must be made small in diameter, soft, and smooth. This can be done by means of a routine which follows:

A. Permanent habit

1. Two regular toilet times daily, never missing, best after breakfast and supper. Unhurried conscientious effort for ten to twenty minutes. (Others between if the urge develops.) If no bowel movement by bedtime secure one by suppository or enema. Never allow child to retire without a bowel movement for the day.

2. Water: Total of one quart daily.

3. Diet: Stewed fruits, generous portions breakfast and supper. Figs, prunes, apricots, best. Some dried fruits to chew between meals. Fibrous vegetables, two generous portions daily. Bran or yeast may be used as desired.

B. Temporary aid

4. Neo-Collagar, or Petrogalar, or Loraga or zymenol (without magnesia, or cascara, or phenolphthalein unless ordered) one teaspoon to one ounce, morning and afternoon, for a few days to start. As habit develops, gradually decrease size of dosage (but continue two a day) until able to do without.

Some proctologists feel that as an initial procedure an evening oil enema retained all night is useful. One of the most helpful means has been found to be training the mother to apply pontocaine or a similar anesthetic and antiseptic ointment to the rectal lining fifteen or twenty minutes before stool time. This is done by means of a rectal nozzle attached to the tube of ointment. Some of the ointment is started out of the apertures in the nozzle, then the nozzle is inserted its full length, then a suitable quantity of additional ointment is squeezed from the tube, then the buttocks are held pressed tightly together and the nozzle is withdrawn with a twisting movement to distribute the ointment as thoroughly and evenly as possible. A relatively painless movement is thereby secured, at intervals frequent enough to minimize stool bulk and dryness. Treatment is twice or three times daily with a generous dose of ointment for the first week or so. After that it is tapered off as to frequency and amount of ointment as improvement takes place, and discontinued when the condition warrants.

External fissures are helped to heal by application of silver nitrate which produces a sterile protective coagulum around which epithelium grows luxuri-

antly. The pure stick may be used, being applied only once for small fissures, repeated as necessary for larger ones. Deep ulcerated ones may also require temporary paralyzing of the sphincter by wide dilation under anesthesia the first time, and possibly even repeatedly. Sulfonamide or other germicidal ointment may be used locally.

Proctitis may require several weeks or even months to clear up. At best it requires as long to heal as a second degree burn of external skin. The more the healing is interfered with by harsh stools the longer it takes. If it shows little progress in two or three weeks it, too, may benefit if in addition to treatment already outlined, it is treated topically with silver nitrate. Even here the pure stick on a carrier may be sparingly used.

Instead of constipation, frequent small but otherwise normal stools may be the complaint. Here again fissure or proctitis, or local dermatitis may be found to be causative, just as cystitis causes frequency of urination. Dermatitis around the rectum may be on a basis of fungus infection, pinworm or scabies infestation, or bacterial cryptitis or papillitis. For fungus one-half or one-third strength Whitfield's ointment, used nightly for a few nights, then alternate nights a few times, then twice weekly for a few weeks, then weekly for a month or two, has been found effectual. In eradicating pinworms, the chief point to be stressed is prevention of *re*infestation. A pad of carbolated vaseline worn over the rectum constantly for a month, beginning at the start of gentian violet treatment and continuing a week or so afterward, has been found to accomplish this. For scabies a single overnight thick application of Danish ointment, from chin and ears down including fingers and toes and genitalia, has been found to be generally effectual, whereas less messy and objectionable treatments have failed. Cryptitis and papillitis require sulfonamide or other antiseptic ointments, and may have to be drained surgically before they will resolve. The possibility of such rare conditions as gonorrheal, syphilitic or tuberculous or diphtheric proctitis must be kept in mind by the pediatrician.

Blood passed by the anus, especially if recurrent, persistent, or chronic, and more especially if bright red, calls for rectal examination. Cherry colored blood, either free, or streaking the outside of the stool usually comes from very low down. That not so bright, particularly if intimately mixed with stool or mucus, usually comes from higher up. The darker the blood the higher its origin in general, but blood from sources quite high up may be fairly bright if the flow is copious enough to bring it through the rectum before oxidizing and other changes have time to take place.

Causes of bleeding visible through the proctoscope are fissure, proctitis, polyp, or ulcer (nonspecific or amoebic). I have even seen the end of an intussuscipiens by proctoscope. It looked and felt like a tiny soft cervix uteri.

If the answer to bleeding is not found locally, the many other causes, including ulcerated Meckel's diverticulum, blood dyscrasia, dysentery, polyp, trauma, infestation, peptic ulcer, tuberculosis, malignancy, hepato- sphenomegalic partial obstruction, esophageal varices, swallowed blood from epistaxis.

bowel obstruction of any variety including intussusception, or mesenteric thrombosis, must be considered.

When the child's rectum prolapses, the pediatrician must determine whether a polyp or other local protruding mass is responsible. If no polyp is present it is usually a matter of redundant, loosely attached lower rectum, forced down by straining to pass a constipated stool.

In immediate treatment, concern should not be so much for prompt reduction, as for permanent retention after reduction. For that purpose, it is advocated by some proctologists that there be no hurry about reduction. If prolapse is allowed to persist for a matter of an hour, or hours, even till spontaneous reduction with simple recumbency takes place, the resulting edema and local submucous reaction is helpful in producing thickening and fibrous tissue production which will help anchor the rectum more firmly in place if stools can be kept thin and smooth enough to pass easily while mucosal edema is subsiding. Various ways are proposed for maintaining reduction, such as continued recumbency, elevated hips, strapping buttocks together with adhesive tape, evacuation by two-way tube, or by enema while lying down, or even vertical suspension of both legs. Of course measures as outlined before, to produce lubricated soft stools, must be instituted concurrently.

Most acute prolapse is self-curative in time, but if conservative treatment fails to prevent recurrences the case is one for injection of quinine urea hydrochloride or other sclerosing solution into the posterior submucous spaces by an experienced proctologist. The older methods of longitudinal cauterization or open surgery are no longer recommended.

A different form of constipation, evidently neuropathological in etiology is that of a child who just never seems to have the urge. Such children are found to have a dilated ampulla, full of rather hard stool, but normal-sized colon otherwise. If such cases are investigated they are usually found to present concomitant abnormalities related to deficient innervation by lower spinal cord segments such as late walking, poor bladder control, and sometimes spina bifida occulta. It is difficult to help these patients because their deficient nerve supply cuts down rectal sensitivity to such a point that a great deal of fecal matter can accumulate without evoking the evacuation reflex. The region is concomitantly atonic, and stretches to large proportions easily. This stretching further reduces local tone, increasing the vicious cycle. Every assistance must be given to promote two or more movements daily, in order to allow the ampulla to shrink to normal size and to gain all possible tone and sensitivity. The constipation routine already given must be rigorously followed, even though it means fairly frequent enemas. Drugs have little or no beneficial effect. Time, growth, and development usually bring about some improvement, but it is so slow and discouraging that these patients often drift from doctor to doctor for years.

An extension of this type of constipation is the megacolon problem. This is not primarily a proctological consideration, but it has been reported

that a certain portion of these cases can be relieved more or less completely by systematic rectal dilation. Even though the rectum is not markedly constricted, easing of its tone by insertion of graduated dilators, beginning with a small size and progressing to large seems to eliminate a causative factor in enough instances to make it warrantable for the pediatrician to try this easy, harmless procedure in all cases before referring them on for sympathectomy or other drastic treatment.

Other major proctological conditions such as peri- or pararectal abscesses, fistula in the anus, and hemorrhoids, are seen occasionally in childhood. They belong essentially to the surgeon, but their medical aspects are not to be neglected.

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THE HETEROPHILE ANTIBODY REACTION IN INFANTS AND CHILDREN

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SINCE Pfeiffer published his monograph on glandular fever in 1889, thus bringing the disease to the attention of the medical world as a distinct clinical entity, many reports of cases and epidemics have appeared in the literature. With the appearance of definite blood changes in these cases later the term infectious mononucleosis has been used in referring to this clinical entity.

The diagnosis of this disease has usually been based on the clinical findings, the appearance of characteristic lymphocytes in the blood, and the positive antibody reaction against sheep cells which was first demonstrated as being present in these cases by Paul and Bunnell.[1] However, in some stages of the disease, the typical lymphocytes have been difficult to demonstrate and much reliance has been placed upon the heterophile antibody reaction for diagnostic purposes.

The term heterophile antibody applies to antibodies having the capacity to react with certain antigens which are quite different from and phylogenetically unrelated to the one instrumental in producing the antibody response. The existence of these antibodies was first recognized largely through the work of Forssman[2] in 1911.

In this paper we do not intend to delve into the complexity of studies involving the development of knowledge of the heterophile antibody reaction, as our principal interest concerns the specificity of the reaction as a diagnostic aid in infectious mononucleosis.

As has been noted previously by Stuart and associates,[3] the importance of this disease should be stressed not only because of itself as a disease entity, but also because the disease must quite frequently be differentiated from lymphatic leucemia. We have also been impressed with the close similarity, clinically, in the picture of infectious mononucleosis in a child and cases of acute upper respiratory infections accompanied by lymphadenopathy and lymphocytosis without the presence of abnormal lymphocytes. Because of the frequency with which the latter picture presented itself, we decided to obtain a heterophile antibody determination on a group of infants and children with such infections and at the same time run a control series of cases without acute infections. Stuart and associates,[3] have questioned whether infectious mononucleosis is a disease entity as it has been generally recognized or whether it is an unusual reaction to an ordinary upper respiratory infection.

Most texts emphasize that the increase in titer of sheep antibodies occurs only in cases of infectious mononucleosis and after the injection of animal serum as shown by Davidsohn.[4, 5] The statement is frequently made that no other condition causes an increase in titer above 1:50 for sheep cell agglutinins. Davidsohn[6] takes a titer of 1:160 as the upper border of normal.

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Although according to these texts the aforementioned conditions are the only ones which may cause an increased titer above these borders of normal, several men in the literature have demonstrated high titer reactions in other conditions.

Bornstein[7] states it is surprising that increased titers of heterophile antibodies are not observed more frequently because it has been shown an ever-increasing number of bacteria contain heterophile antigen. He names among these the Shiga bacillus and several pneumococci and Salmonella types. He reports a case of *Escherichia coli* cultured from the blood of a patient with severe cystitis which contained heterophile antigen. Following bacteriemia, the patient's serum gave a positive heterophile reaction of 1:1,600. The antibodies were of the Forssman type and differentiated from the ones observed in serum sickness and infectious mononucleosis. This he referred to as a false Paul Bunnell reaction.

Bailey and Sharb[8] reported an increase of sheep hemolysins in the serum during the course of pneumonia. Bailey[9] found some relation between heterophile antibody titer in human sera and infections. Bethel and associates[10] state that positive reactions such as Bornstein describes are rare; but that they do occur is evidence that some relation exists between heterophile antibodies in human serums and infections.

Straus and Bernstein[11] found that increased titers of heterophile agglutinins had been reported for the blood serums of patients with serum sickness, pneumonia, scarlet fever, measles, tuberculosis, aplastic anemia, filariasis, and for those of patients treated with quinine or parenteral liver extract. They were, however, unable to confirm these claims and considered the differential absorption test of diagnostic value.

On the other hand, Bunnell[12] asserts that in none of the clinical conditions simulating infectious mononucleosis or those with which it might be confused were they able to demonstrate any appreciable increase in the agglutinin titer. In this article, however, the age range of these patients is not mentioned.

The agglutination test for infectious mononucleosis has become widely used as a diagnostic test and it has been generally agreed that an increased sheep cell agglutination titer is strong evidence of the disease providing that serum sickness can be excluded. It is, we feel, not generally realized on the part of many clinicians that a positive titer above the so-called upper border of normal may present itself in other than the aforementioned conditions.

Barrett[13] feels that the difference of opinion as to the proportion of cases of glandular fever having positive agglutination tests may be due to the unwitting use by different workers of different standards in the agglutination tests.

Stuart and associates[3] demonstrated there is general disagreement in the literature concerning the sheep cell agglutinin titers of normal people and the results reported depend to a large extent on the technique used in performing the test. Barrett,[13] after determining titers on 100 apparently healthy people and using the technique of Stuart and associates,[3] compared his results with theirs. As is shown in Table I, his results were quite different.

TABLE I

	NO. OF TESTS	TITER LESS THAN 1:10	1:10	1:20	1:40	1:80	1:160	1:320	1:640
Stuart and associates	300	3.00	23.00	46.33	20.66	6.00	0.66	0.33	0
Barrett	100	90	9	1	0	0	0	0	0

(Final concentrations: 0.5 per cent cells 37° C.)

Barrett states that using his own normal standard he might have found the sheep cell agglutination test satisfactory for glandular fever but if he used Stuart's figures, he would have obtained a smaller proportion of positive reactions. He was unable to account for the difference in results but it is interesting that he noted that all of his patients were healthy people whereas Stuart's patients had various types of diseases. However, Bunnell[12] found no significant differences in patients with such diseases and in normal people.

In our group of children there was apparently a definite difference in the group of cases with infections as compared with the healthy individuals.

Another aid in differential diagnosis of infectious mononucleosis has been suggested by Bailey and Raffel[14] and Davidsohn.[15, 16] This is referred to as the absorption test. By this they demonstrated the heterophile antibody could be absorbed almost completely from the serum by sheep and ox cells but it was not at all absorbed from the serum by guinea pig kidney tissues which contain the typical Forssman heterophile antigens. From this they concluded that the heterophile antibody of infectious mononucleosis was not the same as the Forssman type and that the diagnosis of infectious mononucleosis could be aided by performing the absorption test with both the ox erythrocytes and guinea pig kidney.

The principle of the Davidsohn differential test depends on "the failure of the emulsion of guinea pig kidney to absorb more than 75 per cent of the heterophile antibodies from the serum of patients with infectious mononucleosis," whereas the emulsion of boiled beef erythrocytes will completely absorb them. If 90 per cent or more of the agglutinins are removed by the emulsion of guinea pig kidney, it is said to speak against infectious mononucleosis.

This test was not used in our series of cases and so far as we know has not been used routinely in many institutions. It seems as though it would prove of value providing other infections may not react as the infectious mononucleosis cases.

Since, in some cases, apparently the diagnosis of infectious mononucleosis is being made principally on the presence of an elevated heterophile antibody titer without the presence of abnormal lymphocytes, we should like to stress the fact that we feel such a diagnosis should not be made on the basis of an elevated titer alone.

Because of the marked similarity of cases with upper respiratory infections accompanied by lymphadenopathy and the clinical picture presented by many cases of infectious mononucleosis, we felt it might be of interest to obtain routine heterophile agglutination tests on a series of patients with upper respiratory infections in St. Louis and vicinity during the winter of 1944-1945. These patients

were admitted to the hospital from adjacent communities within a radius of approximately 100 miles. So far as we knew, there were no large number of definitely diagnosed infectious mononucleosis cases in this community at this particular time.

Some of these children had a lymphocytosis which one might normally expect to be present in the very young age group, but which in some cases presented itself also in the age group over 2 years. None of the abnormal cells classified as the type present in infectious mononucleosis were noted. A large percentage of these children had a definite lymphadenopathy as noted in Table II. We were unable to determine whether the blood changes and adenopathy noted were due to the infection or might possibly have been associated with the sulfonamide therapy which the great majority of them received.

TABLE II

AGE	NO. OF CASES	AGGLUTINATION OVER 1:160	MAXIMUM AGGLUTINATION	PERCENTAGE OVER 1:160	LYMPHADENOPATHY
Control Cases—No Infections					
Under 1 year	8	0		0	None
1 to 2 years	5	0		0	None
2 to 12 years	25	1	1:320	4	9
Cases With Upper Respiratory Infections					
Under 1 year	39	4	1:2560	10	5
1 to 2 years	32	6	1:1280	18	14
2 to 12 years	47	7	1:640	14	29

Diagnoses in these infections were principally: acute otitis media, acute laryngitis, acute tracheobronchitis, and pneumonia. Predominating organisms were the pneumococcus. *Hemophilius influenzae,* and *Micrococcus catarrhalis.*

The heterophile titers in a number of these cases were definitely elevated above the level of what was considered as the upper border of normal for the particular method by which the test was being run. A control group of patients without infections was run and in only one case, which was a skull fracture, was a 1:320 titer obtained.

Due to factors beyond our control, it was sometimes impossible to follow up with check tests over a long period of time on some of these patients, but we were able to obtain at least one repeat test and in many of the cases several titers were obtained.

As stated previously, the so-called normal titer is dependent upon the method of preparation and titration and the upper border of normal apparently ranges from 1:64 to 1:160 depending upon the method used. The routine followed in our series is a modification of Davidsohn's technique, in which a titer of 1:160 is considered strongly suggestive of an appreciable increase in nonspecific heterophile antibody level in the blood.

Routine heterophile determinations were done on 156 infants and children between the ages of 2 weeks and 12 years. Of these, 118 cases had acute infections and 38 were children without evidence of infection and who, so far as

we could determine, had received no recent serum injections. Only one child in the control group as mentioned previously presented a titer of 1:320.

It was noted that many of the cases presenting the higher titers appeared during the height of the epidemic of the upper respiratory infections from about the middle of January to the middle of February.

One child demonstrated a rise in titer from 1:160 to 1:320 after the administration of plasma on two separate occasions.

We divided the cases into age groups since we felt there might be some difference in the antibody reaction in the various groups.

None of the lymphocytes in these cases were of the type noted as being present in infectious mononucleosis. In none of our series of cases was splenomegaly present at any time. We again want to call attention to the fact that the majority of the infectious cases were on sulfonamide therapy and we have frequently observed an adenopathy and lymphocytosis develop while children received sulfonamide therapy. Whether this was responsible for the lymphocytosis and adenopathy in our series we cannot say. We also do not know what effect, if any, it may have had on the heterophile antibody reaction.

Naturally the question arises as to whether these cases with increased titers were possibly cases of infectious mononucleosis. As was mentioned previously, no abnormal lymphocytes and no splenomegaly were present. The occasional lymphocytosis and the adenopathy noted in some of our patients with high titers were also present in some of the patients who had negative or low titers on frequent heterophile determinations. This is brought out in Table II in which cases with palpable lymph glands outnumbered these cases with increased titers, particularly in the older age groups.

Clinically, all of the patients with the acute infections presented much the same picture usually seen in acute upper respiratory infections during the winter months. This was true of the entire group with both high and negative titers.

SUMMARY

We present heterophile antibody agglutination results on 156 patients, 38 of which were controls, in the age range from 10 days to 12 years. The control group was free of any acute infection, while the others were cases of acute upper respiratory infections admitted to the hospital during the winter of 1944-1945. Lymphadenopathy was noted in a large number of cases but no splenomegaly was found at any time. Differential blood studies revealed no atypical mononuclear cells as are found in infectious mononucleosis. A titer above the accepted normal of 1:160 (using Davidsohn's technique with slight modifications) was found in an appreciable number of cases of upper respiratory infections, while only one control revealed a titer above 1:160.

The literature is briefly reviewed to show questions raised against accepting high antibody titers as positive evidence of infectious mononucleosis in cases not presenting the so-called "atypical mononuclear cells," and the suggestion offered by some authors that other conditions than infectious mononucleosis may cause high heterophile titers is brought out in the results on the 128 cases of upper respiratory infection the authors tested for heterophile agglutinins.

CONCLUSIONS

1. Heterophile antibody reactions have been reported in concentrations above the accepted normal in various cases of upper respiratory infections in children in an appreciable number of cases.

2. Too much stress should not be placed on the diagnostic value of the heterophile antibody reaction in infectious mononucleosis without the presence of abnormal lymphocytes found in infectious mononucleosis.

3. A standardized technique should be adopted by various institutions for running heterophile agglutination tests in order to interpret better the results obtained.

4. The sulfonamide drugs used in these cases may possibly have altered the antibody reaction.

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508 NORTH GRAND BOULEVARD

SEDATIVES AND STIMULANTS IN PEDIATRIC PRACTICE

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WHEN I began putting together some views on the use of stimulants and depressants or sedatives in pediatric practice it seemed a good plan to try to relate them to what pediatricians have thought about these subjects. I looked through the usual repositories of considered opinion, the textbooks. I was disappointed indeed to learn how scant were the revelations of pediatric views on these matters. The 1940 edition of Holt and McIntosh[1] among 1421 pages of pediatrics doesn't list the term stimulant in the index. There are the terms sedatives and sedation in the index, but they only refer back to two lines about their need in pneumonia and a few lines about the tolerance to and dosage of phenobarbital. I did not meet with much better success in the several other reference texts on pediatrics which I consulted.

I wonder whether the rather meager attention which these subjects appear to have received from pediatricians does not reflect the view that they have been fairly well covered in writings on adult medicine or textbooks of pharmacology.

There is evidence of this dependence in the traditional outlines of dosage in children. If we want to learn the dose of a drug in adults we give it to some people in varying amounts and under varying conditions. Ultimately we arrive at some notion of how much the average person needs for the various purposes. That isn't what is usually done in the case of children. Here we first obtain the adult dose and then divide it by a number. I do not quite see why pediatricians have tolerated this practice so long. I am sure that internists would not for a moment countenance the reverse practice, namely, to determine the dose for a 5-year-old child and then multiply it by a number to obtain the adult dose, although it is quite as easy to multiply as to divide.

I know of an argument against this stricture, namely, that the adult dose is more stable, while the child is forever in transit, from a small and light person to a larger and heavier one. But that is not quite enough. I believe that the pediatrician would be the first to protest that an infant or a child is not simply one-fifth or one-third of an adult. He is something different. His surface area is relatively great, his basal metabolism rapid, his liver large, and his urine secretion high. These are all factors which might influence his response to a drug.

The literature is replete with clear statements and contradictory ones, that children are more susceptible to some and less susceptible to other drugs than adults. As to the proof, the pediatric writings refer us to the statements in textbooks of pharmacology, and the later in turn send us back to the pediatricians as the authorities.

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There are many experimental studies in animals of the relation between dosage and such factors as age, weight, size, and surface area. The results are fragmentary and often contradictory. The relationships are complex. There is not enough information to be quite certain as to what general laws are applicable to children.[2] While there have been some pharmacologic investigations in infancy and children,[3] there is little doubt of the need of more systematic study of dosage of drugs in children with the view of ascertaining by direct observation the smallest amounts necessary to attain specific objectives. I am inclined to believe that drug therapy in children is suffering from an adult orientation.

SEDATIVES AND HYPNOTICS

The more important sedative agents are the barbiturates, chloral hydrate, acetylsalicylic acid, the bromides, and paraldehyde. All of these substances depress the brain. They raise thresholds. They produce changes in the sensory, motor, intellectual, autonomic, and psychic reactions. They depress reflexes. There is no reason to suppose that any portion of the brain escapes their action. The net result is an altered nervous state which varies greatly from person to person and also with the size of the dose.

In general, they tend to produce a feeling of lassitude, diminished mentation, a disinclination to mental and physical exertion. This type of action is often associated with release from a state of anxiety and disturbing sense of unrest. It is for this action that adults turn so frequently to this group of agents. A dose two or three times a day enables them to function more comfortably and efficiently. They take it for long periods of time, sometimes for months or years.

While this type of action probably provides the largest field of usefulness of the sedative agents in adult practice, I believe its application is relatively infrequent in pediatric practice.

I call attention to this difference because it has a bearing on another problem. The sedative dose for the ambulant adult is very small. It serves merely to reinforce the will to rest, and at night when other conditions are conducive to sleep it may promote sleep. Wakefulness and excitement are, however, within the patient's control. Without the patient's cooperation, and under the influence of stimulation, the depressant effects of these doses may be quite completely obliterated.

The next step in the control of excitement and unrest in adults is the use of these materials as chemical restraints. The patient's cooperation is here relatively unimportant. The doses are very much larger. Their field of application is the patient who is ill in bed, the unrest of severe infections, coronary thrombosis, or postoperative unrest. This type of application of sedative drugs is suitable chiefly for short-range problems. I believe that candidates for sedatives among infants and children fall mostly into this group, namely, bed patients, large doses, short periods of treatment.

There are hazards in this use of the sedatives as chemical restraints. They promote constipation and abdominal distention. They may interfere with

sweating and with normal temperature control. During the process of recovery from the subanesthetic stupor, there is often a confusional state with troublesome unrest. There is also the fact that the protracted use of the barbiturates tends to produce a state of excitability of the central nervous system which may lead to a fit when the drug is withdrawn. This has been noted especially in the treatment of epilepsy.

As to the tolerance of infants and children to the sedative agents, the recent textbook on pharmacology by Goodman and Gilman (1940)[4] states that, as a rule, children are more sensitive to drugs than adults and that infants are abnormally sensitive to depressants of the central nervous system. In the same year there appears in Holt and McIntosh (1940)[1] the statement that the barbiturates are among the drugs to which infants are tolerant.

The preponderance of experience, I believe, favors the view that children require proportionately larger doses of sedative agents to quiet them than adults. What precisely is the meaning of this? Does it signify that the brain cells are less sensitive so that more drug is necessary to affect each cell? Or is the rate of destruction so rapid that an equally effective concentration can only be reached by larger amounts than in adults?

I have already indicated that in response to sedative agents, children offer little cooperation. They behave toward these agents like excited or manic states in adults. In order to quiet them it is necessary, as in the case of these adults, to use the dosage range of the chemical restraint. When these comparable conditions are now related, the susceptibilities of the child and adult do not appear to be materially different. In the use of sedatives as chemical restraints, children and adults seem to require substantially similar doses per kilogram of body weight.

A clear understanding of this matter is now particularly important in the light of the growing use of barbiturates, such as pentothal sodium, for full surgical anesthesia. It has been stated that children require twice as much pernocton per kilogram as adults for narcoses.[5] Under the conditions of surgical anesthesia the margin of safety is small, and I believe it would not be wise without further evidence, on the assumption that children are more tolerant than adults, to give an infant of six months weighing about 7 kilograms, one-fourth of the adult anesthetic dose as is recommended in the case of sedation.

Are there any qualitative differences in the action of the various sedative agents? How shall we decide which to give and when? There is experimental evidence that the pattern of their actions is not the same. Studies on animals indicate, for example, that phenobarbital is a relatively more active depressant of the motor cortex than other barbiturates, that amytal blocks the vagus peripherally while phenobarbital does not, that chloral may disturb postural reflexes without sleep, while barbital may produce sleep without disturbing postural reflexes. Facts such as these suggest that there might be some clinical conditions which would be more favorably influenced by one of these than by another. But what these clinical conditions are or even whether they exist has not been determined for either adults or children.

There are many individual preferences and there is a marked tendency to shift from one preparation to another if the results with one are not satisfactory. The clinical testimony in regard to qualitative differences is, for the most part, intangible and contradictory. The techniques of scientific clinical investigation have never been put to work on this subject.

For routine purposes in which a sedative agent is necessary, I usually recommend phenobarbital for oral administration or the sodium salt for injection. Unlike the scores of other barbiturates, its solution is not strongly alkaline, but nearly neutral, and may be given subcutaneously without local irritation.

Phenobarbital is a long-acting drug. There are occasions, especially in the treatment of convulsive states when a shorter acting one is desirable. These needs are satisfactorily met by the official preparation of pentobarbital-sodium which may be given by oral administration or intravenous injection. Should the dose necessary to control the convulsions prove to be fairly large, it has the advantage that the period of narcosis will not be unduly prolonged.

It may be necessary to abandon the barbiturate in a particular case because it leads to excitement instead of sedation, because it produces a skin eruption, or other signs of intolerance. In that case acetylsalicylic acid, chloral hydrate, bromides, or paraldehyde may be tried. The unpleasant taste and irritant properties of chloral may be overcome by copious dilution and any one of several aromatic vehicles, or by rectal administration in milk. In connection with the bromides one should always bear in mind the fact that they are among the most cumulative of all drugs. It takes from two to three weeks to excrete a dose, and its continued administration leads to toxic levels of bromide in the blood.

Failure to obtain the desired results with one or the other of these agents is likely to be due to the fact that the dose is too small or too large or that the interval between doses is too long or too short. If, after suitable adjustments are made, the results are still short of expectation, I should strongly suspect that the problem is one which no sedative will solve.

MORPHINE

A great deal of emphasis has been placed in the older literature on the dangers of morphine and other opium derivatives in infants and children. The textbook of Goodman and Gilman in 1940 cited the case of morphine as a special example of hypersensitivity of infants to depressants of the central nervous system. Opinion seems to be heavily weighted in favor of this view but the evidence leaves much to be desired. A paper by Schwahn in 1940[6] is a fairly good example of the quality of the evidence. He undertook to make out a case for the great danger of morphine in infants due to what he believed was the inordinate susceptibility of the respiratory center. He cited a case of a 3½-year-old child, weighing let us say about 15 kilograms. He was admitted to the hospital by the family physician who stated that he had given a hypodermic injection of 3 mg. of morphine hydrochloride. This dose is about 0.2 mg. per kilogram which is equivalent to a fair-sized, but safe dose for a man, namely, ¼ grain or 15 mg. The child developed pronounced stupor with respiratory depression and died in convulsions with respiratory failure twelve hours later. The

morphine was given for an attack of severe dyspnea and unrest due to an attack of asthma. When the depression seemed unduly marked, an attempt was made to combat it by two hourly doses of about 0.2 mg. atropine, doses which are the adult equivalent of 1/60 gr., and 5 mg. doses of "lobelin," in addition to 250 mg. doses of "coramin." There are several questions here. Is this an example of hypersusceptibility of children or the danger of morphine in bronchial asthma? What killed the child, the morphine or its combination with the antidote since large doses of atropine are synergistic with morphine? The author warned against the use of more than 0.02 mg. of morphine per kilogram in infants, but then proceeded to recommend doses of from 2 to 4 drops of the tincture of opium, representing about 0.6 mg. of morphine, for infants, which is about five times as much morphine as the dose he had set as a limit. As to codeine, he considered it safer and recommended doses which on the basis of body weight are equivalent to about ¾ grain or 45 mg. for the adult.

Most of the evidence concerning the greater susceptibility of infants and children to morphine is little more convincing than this.

The subject of tolerance was investigated directly by Irish in 1935[7] in a group of infants under 4 months of age. He found that camphorated tincture of opium or paregoric caused mild drowsiness and somnolence without any toxic effects in doses of 0.3 c.c. or 5 minims per pound. This is equivalent to about 0.25 mg. of morphine per kilogram or the average adult dose of ¼ grain. He observed toxic depression after doses about four times as large. Others have also recently taken issue with the prevailing view that morphine is dangerous in infants.[3]

The present indications are that infants and children have about the same order of tolerance to morphine as adults on a body weight basis. A dose of 0.25 mg. per kilogram constitutes a fairly large dose. Considerably smaller ones relieve pain, and as little as 0.02 to 0.03 mg. per kilogram is very effective against cough.

Where morphine is used, I have been impressed with a lack of care in the selection of the dose, with a tendency to use doses much too large and much more than is necessary. This applies to adults as well as to children.

STIMULANTS

We may now turn to the subject of stimulants. The term depressant is usually applied to agents which reduce the activity of the central nervous system. The group of "stimulants" is pharmacologically more heterogeneous. In the choice of a drug for a case in question, we have first to decide what it is that requires stimulation, the cerebral cortex, the respiratory center, the vasomotor center, or the peripheral blood vessels.

I need not tell this group that that decision is not always easy to make. These measures are often applied in urgent situations. In some cases all the systems have been directly damaged by some infection or toxin. In others, a primary failure of the heart or peripheral vasomotor mechanism has given rise to a cycle of disintegration in which the picture becomes complicated by coma, failure of respiration, and the failure of other functions. The fact still remains

that the discernment of the proper target will decide the use of the most effective drug for there are no so-called stimulants which embrace them all.

The agents which are usually placed in this group are caffeine, strychnine, camphor, alpha-lobeline, epinephrine, and other sympathomimetic amines, metrazol, nikethamide (coramine), picrotoxin, and digitalis.

Camphor has been widely employed as a stimulant in circulatory failure. Large doses stimulate the cortical centers giving rise to convulsions. There is a large conflicting pharmacologic literature concerning its action on the blood pressure and the heart. The most recent study from our laboratory using the papillary muscle of the heart shows that camphor does not exert any action on heart muscle to increase the force of contraction. The Council on Pharmacy and Chemistry of the American Medical Association[8] recently re-examined the evidence for camphor as a circulatory, respiratory, or cardiac stimulant. It is extremely doubtful whether camphor exerts any important systemic actions in doses short of those causing convulsions. Claims for it as a stimulant are no longer acceptable.

Strychnine is another belonging to the same category. It has no direct action on the heart. It lowers the threshold of the synapse in the central nervous system. The first detectable action in animals is the "startle" reaction. Its typical action is the spinal tetanus. It stimulates the respiration and vasomotor center only in convulsant doses. The survival qualities of this drug as a respiratory and circulatory stimulant are truly remarkable in the face of the almost complete absence of evidence that it produces either respiratory or circulatory stimulation in doses short of those which cause convulsions.

Considerable interest has developed in the possibilities of alpha-lobeline as a respiratory stimulant. It has been urged as a means of resuscitation of newborn infants, and as a central stimulant in states of depression by narcotic drugs. Its action is similar to nicotine. It produces intense stimulation of the respiratory center, but this action is very brief, lasting only a few minutes. There is also the fact that the stimulation is sometimes followed by a secondary depression. The drug is very capricious. In mild states of depression, it will sometimes increase the respiration, but in states of advanced depression, its stimulant action is often absent and lobeline may contribute to the depression. The properties of lobeline do not justify dependence upon it as a respiratory stimulant.

Where there is need for respiratory stimulation one might turn to caffeine. It may be given in fairly large doses of the order of 10 mg. of caffeine sodium benzoate per kilogram by intramuscular injection. Such doses may be repeated several times at intervals of from thirty minutes to an hour until distinct signs of improved respiration appear. The intervals may then be prolonged and the doses reduced in the endeavor to maintain the effects. Caffeine has the advantage over other respiratory stimulants in that it seldom causes secondary depression.

Caffeine is also frequently employed as a cardiac and circulatory stimulant. It is of questionable value for this purpose. The recent studies with the papillary muscle of the heart show that, in therapeutic concentrations, its action

in increasing the systolic force of the heart is negligible. Therapeutic doses rarely elevate the blood pressure. It tends to increase the metabolic rate and whatever increase in cardiac output results from caffeine may be secondary to the primary increase in metabolism. Its use, therefore, as a cardiac stimulant may promote cardiac exhaustion.

Caffeine exerts a stimulant action on the central nervous system which has some value in depressed states, but as an antidote to narcotic poisons, it is quite inferior to other measures.

If the chief problem is one of vasomotor depression, the most serviceable materials are the sympathomimetic amines. They are applicable to those conditions in which there is urgent need for sustained vasopressor action, either to overcome or to prevent vasomotor collapse. This does not include true shock; here vasoconstriction is already present and the primary difficulty lies in the capillary bed and deficient circulating blood volume. The type of condition in which the vasopressor stimulant is likely to prove effective is often encountered in depression states occurring during anesthesia and in some phases of severe systemic infections.

Epinephrine has been utilized for this purpose but some of the newer amines are preferable. The materials of choice are neosynephrine or paredrine. An intramuscular injection of 0.1 mg. of neosynephrine or 0.2 mg. of paredrine per kilogram produces a very prompt and marked rise of the blood pressure which may then be maintained by repetition of the doses as necessary. They have the advantage over epinephrine in that they are less likely to cause the acceleration of the heart, the pallor of the skin, and the restlessness produced by epinephrine. In point of fact, these compounds are more likely to produce a beneficial slowing of the heart in association with the rise of the blood pressure.

Metrazol and nikethamide are of no value as cardiac stimulants. Papillary muscle experiments show that these compounds do not increase the systolic force of the heart's contraction. Their stimulant action on the vasomotor and respiratory centers often improves respiration and elevates the blood pressure. These actions as well as their stimulation of the cortical centers have been put to good use in the treatment of poisoning by anesthetics and hypnotics. Metrazol may be given in doses of 2 mg. per kilogram intramuscularly and nikethamide in doses of 5 mg. per kilogram intravenously or intramuscularly. The doses may be repeated at one-half-hour intervals until evidence of excitation is present. Great caution is necessary because these are convulsant agents and there is marked individual difference in response. I have seen several instances in which the use of metrazol as a respiratory stimulant gave rise to a convulsion without any significant improvement in the respiration.

Picrotoxin is the drug of choice as an analeptic in barbiturate poisoning. It counteracts the depression of the cortex and respiratory center caused by these drugs. It is not useful as a general respiratory stimulant. In unanesthetized states there is no respiratory stimulation until convulsant doses are given. In barbiturate poisoning doses of 0.2 mg. per kilogram may be given

intramuscularly every fifteen minutes until signs of excitation are present in the form of muscular twitchings. Consciousness is not restored even with convulsant doses. For this we wait until the barbiturate is excreted. Again, caution is necessary to avoid producing convulsions with the picrotoxin.

Where the essential difficulty is cardiac failure, the digitalis glycosides should be used. No drugs known have the power of these to produce sustained increase in the systolic force of the heart's contraction. The material of choice for the acute case is ouabain; an intramuscular or intravenous injection of a full safe dose of 0.01 mg. per kilogram. The use of digitalis presents a somewhat special problem and its further discussion would take us beyond the scope of the present subject.

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CHOREA IN THE NEGRO RACE

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ABOUT seventy-five years ago, Dr. Weir Mitchell published a discussion of chorea, one portion of which concerned the occurrence of that disease in the Negro race.[1] Because it had been incorrectly assumed that hysteria did not occur in the Negro, Mitchell sent a questionnaire to many southern physicians asking that they report to him the approximate number, if any, of cases of chorea seen in Negroes, for at that time it was belived that the disease was not seen in this race. The replies suggested that whereas chorea did occur in the Negro, it was indeed a rare instance when the practitioner was confronted with this disease in a Negro patient, and rarer yet if the afflicted individual were not a mulatto. Many other brief reports[2-5] were published during the next five years of an occasional case or two, but interest in this phase of chorea seems to have decreased in the interval between Mitchell's report and the present time. However, in 1933, Lueth and Sutton[6] published a review of the records at Cook County Hospital, the results of which are given in Table I. These authors summarized their report by stating that, although their clinic was composed of a "select cardiac" group, that the incidence of chorea was about the same in both the white and the Negro race.

A personal interest in the incidence of chorea in the Negro race came about when a fatal case of chorea was seen in a Negro girl 11 years of age. Because fatalities in chorea are so rare, it was felt that this case should be reported, and during the preparation of the review it became apparent that much interesting and perhaps valuable material could be collected by making a survey of the number of cases of chorea seen in Negroes by southern pediatricians. It is the purpose of this paper, therefore, to report first the case mentioned and then the results of the survey.

CASE HISTORY

F. M. S., an 11-year-old, apparently full-blooded Negro female, was admitted to St. Margaret's Hospital July 9, 1943. The father stated that the girl had been well until approximately ten days before admission to the hospital. At that time, he noticed that she had "twitching movements" of the extremities which eventually involved the entire body. For one week, the child had been unable to feed herself. The past history was noncontributory. The patient was in the fifth grade of school and made excellent grades.

On physical examination, the patient was of average height and weight. No significant findings were present except in motor activity of the body. The child was unable to remain quiet. She was cooperative, but the body and extremities were constantly in motion—useless, purposeless, nonstereotyped movements. Facial grimaces were present. No sensory loss or decrease could be demonstrated. All reflexes were present but depressed. The diagnosis was typical Sydenham's chorea.

The course of the illness was one of progressive severity. The movements became increasingly active until the child was almost thrown from the bed regardless of usually

From the Pediatric Service of St. Margaret's Hospital.

TABLE I

	WHITE		NEGRO		TOTAL
	MALE	FEMALE	MALE	FEMALE	
Rheumatic fever	31	31	8	13	83
Chorea	22	27	4	5	58
Miscellaneous	8	12	1	3	24
Total	61	70	13	21	165

From Leuth and Sutton.[8]

adequate doses of phenobarbital. The temperature which had been normal, slowly began to rise to 102° F. ten days after admission and continued to fluctuate for four days. At this time, the movements constituted chorea insaniens and the sedation had been greatly increased; all feedings were by gavage, and no new physical findings were present. Fifteen days after admission to the hospital, the temperature rose suddenly to 109° F. where it remained until the patient's death approximately twelve hours later. At no time were there any significant heart findings.

Laboratory Data.—Blood Count:

July 9. Red blood cells, 3,700,000; hemoglobin, 11 Gm.; white blood cells, 8,750; polymorphonuclears, 75 per cent; lymphocytes, 25 per cent.

July 21. Red blood cells, 3,850,000; hemoglobin 11.5 Gm.; white blood cells, 7,900; polymorphonuclears, 70 per cent; lymphocytes, 30 per cent.

Urinalysis:

July 9. Straw colored, cloudy, acid, specific gravity, 1.029; albumin, negative; sugar, negative; pus cells.

Stool:

July 9. No ova or intestinal parasites found.

Spinal Fluid:

July 20. Clear, colorless. Not under increased pressure. Pandy negative; qualitative sugar positive, no cells found.

Kahn:

July 25. Negative.

Sedimentation rate:

July 12. 10 mm. in 1 hour.

Autopsy Findings.—The only significant findings were limited to the lungs, heart, and brain. The left lung showed moderate patchy consolidation of the lower lobe. The heart was of normal size. On opening the heart, the muscles were firm; the edge of the mitral valve was slightly roughened. The other valves were thin and intact. On opening the head, the cortical surfaces of the brain were markedly congested. The hemispheres were symmetrical as were the pons and medulla. On section of the brain no significant findings were present other than some perivascular congestion.

DISCUSSION

Undoubtedly the individual who expects medicine as a whole to be of the same degree of accuracy as a biochemist's titration will be quite disappointed in the results of this survey. However, everyone engaged in private practice, and especially so during the war years, knows that it is almost impossible to keep accurate filing of cases or to study the records to obtain a true summary of those cases. The same inaccuracies of Mitchell's report are to be found here. There is, however, one difference. In reviewing several of the replies sent to Mitchell there seems to be some doubt as to the proper diagnosis of chorea.[3] It was determined in the present survey to send the questionnaire, "How many

cases of chorea in the Negro race have you seen?'' to all members of the American Academy of Pediatrics in Region II which comprises the South. It was felt that although the general practitioners in the rural areas of the South had the greater opportunity in seeing chorea in Negro people that it would be impossible to write each physician and that the pediatricians would provide a more accurate diagnostic series.

TABLE II

STATE	QUESTIONNAIRES SENT	NUMBER REPLIES	NUMBER CASES REPORTED*	REMARKS
Alabama	15	10	11	7 of these seen at Hillman Hospital over a period of 20 years
Arkansas	3	2	0	
Florida	22	7	0	
Georgia	26	9	10 to 15 (?)	Many doctors ''guessed'' about number seen
Kentucky	7	4	0	One doctor reported ''have never seen a case in Kentucky but had 2 in Philadelphia''
Louisiana	23	12	2	One reported ''not a mulatto, severe case''
				One stated ''saw 2 in Boston and 1 in Philadelphia''
				One remarked ''saw 2 in Cincinnati, but none since coming to Louisiana''
Mississippi	8	4	0	Of the doctors reporting, 3 had been in their present locality 12, 15, and 10 years, without seeing a case of chorea in Negro
North Carolina	17	16	28 to 32	2 stated occurred in mulatto children
				2 cases in twins; illnesses 1 year apart
Oklahoma	11	5	5	See reports of cases in hospitals
South Carolina	10	5	6 to 12	One doctor reported ''think I have seen about 6 cases in 12 years''
Tennessee	22	9	6 to 7	One doctor reported ''the case I saw was extremely severe''
Texas	48	24	19	See reports of cases in hospitals
Virginia	20	10	6	One patient had frequent recurrences.
West Virginia	5	3	1	

*Number of cases reported should be compared with cases seen in hospitals as in Table III.

Slightly more than 50 per cent of the pediatricians in Region II found the opportunity to reply. The results are summarized in Table II. It is evident from this table that in the larger cities the number of cases may be even more inaccurate than the figures of the smaller towns, for the cities usually have hospitals with relatively large services, and several attending pediatricians may have seen the same cases that his colleagues reported. Several men were kind enough to provide the figures of hospitals in their communities although no request for this information was made. A summary of these hospital reports is given in Table III.

Except for Texas, which characteristically has the largest of everything, North Carolina led the number of replies. The latter state reported thirty-two cases of chorea, which exceeded that of all other states concerned. One pediatrician in North Carolina reported that as nearly as he could recall, he had

TABLE III. NUMBER OF CASES OF CHOREA IN NEGROES REPORTED IN SOUTHERN HOSPITALS*

STATE	NUMBER OF CASES REPORTED
Alabama	
Hillman Hospital	7 cases in 20 years
Georgia	
Grady Hospital	6 cases
Louisiana	
Charity Hospital	None from Jan. 1, 1942, to Sept. 25, 1944, which represents 28,562 Negro male and 44,020 Negro female children examined†
North Carolina	14 cases: 10 girls, 4 boys, aged 7 to 14 years
Duke University Hospital	
Oklahoma	3 in 10 years; during same period 96 white children
University Oklahoma Hospital	had chorea
South Carolina	4 cases in 9 years; aged 15, 15, 14, 10 years
Roper Hospital	
Tennessee	15 cases in last 10 years; ages from 3 to 15 years,
John Gaston Hospital	seven males, eight females
Texas	
Parkland Hospital	1
Freeman Clinic	0
Children's Medical Center	5 cases in eight years; 20 cases in white children during same period
University Texas Hospital	3 cases in nine years; 14 cases in white children during same period.

*All figures are direct from physicians and not given as official by hospital authorities. No request was made direct to hospital but information voluntarily obtained by pediatrician queried as to number of cases he had seen.

†Provisional survey.

seen only three cases of chorea in Negro children in nineteen years of pediatric practice and that two of those were in mulattoes. Another of the same state reported three cases in twenty years, two of whom were twins who had the disease about a year apart. Texas and Alabama were second and third, respectively, following which the remaining states reported few cases.

This information gives rise to many questions as yet unanswered. In Mitchell's report, he mentioned that Dr. Michel of Montgomery, Ala., stated that none of the thirty members of the county medical society had ever seen a case of chorea in a pure-blooded Negro although the disease was encountered in the white race. At the present time, a survey of the members of the county medical society of Montgomery, Ala., reveals that the members have seen only two cases, including the case reported in this paper. Mitchell further stated, "Dr. Benjamin Lee writes that in a year of service in the Hospital of the Home for Colored Children, New York, he saw a case of chorea in a mulatto girl, aet. 15 end fatally, but has never seen it in the pure black." This statement gives rise to two questions: Is chorea less common in the pure Negro and is chorea more severe in the Negro than in the white race? There are, of course, no accurate figures to answer either question, but as to the purity of race one can at least attempt to correlate the results given in Table II with the per cent of Negro population of the various states as given in Table IV. It is generally believed that there are more "pure" Negroes in the "deep South" than in the more northern states, and this can be easily believed after a trip through North and South Carolina as compared with southern Alabama

TABLE IV. NEGRO PER CENT OF POPULATION

STATE	1900	1920	1930	1940
Mississippi	58.5		50.2	49.2
South Carolina	58.3		45.6	42.8
Louisiana	47.1		36.9	35.9
Georgia	46.7		36.8	34.7
Alabama	45.2		35.7	34.7
Florida	43.7		29.4	27.1
Virginia	35.6		26.8	24.7
North Carolina	33.0		29.0	27.4
Arkansas	28.0		25.8	24.7
Tennessee	23.8		18.3	17.4
Texas	20.4		14.7	14.4
Delaware	16.6		13.7	13.4
Kentucky	13.3		8.6	7.5
West Virginia		5.8	6.6	6.1

and Mississippi. In comparing these states' reports and Negro population, there were no cases of chorea reported by four pediatricians in Mississippi which has 49.2 per cent Negroes; Alabama, with a colored population of 34.7 per cent, reported eleven cases in ten replies. North Carolina, with 27.4 per cent Negroes, reported thirty-two cases in sixteen replies, and South Carolina reported approximately twelve cases, five replies, in a population of 42.8 per cent Negroes. It is at once evident that few replies were received from Mississippi and South Carolina, the states with the highest Negro population. However, in approximately the same number of reports from those two states no cases were observed in Mississippi and about twelve were seen in South Carolina. No conclusion can definitely be drawn from this comparison, but one can only wish that the general practitioner of Mississippi who sees the majority of colored patients could report his findings.

In attempting to discuss the severity of chorea in the Negro, several of the pediatricians in the survey reported their cases and added that the disease was extremely severe, as it was in the fatal case which I have reported. If chorea is more severe in the Negro, the explanation is difficult. Almost all southern physicians will agree that the majority of diseases attributed to the streptococcus are usually mild in the South. Scarlet fever is usually extremely mild with few complications being reported. Rheumatic heart disease is infrequent, and in several localities I have heard pediatricians discussing the problem of rheumatic fever remark that often the cases were so mild as to make the diagnosis uncertain. These remarks were applied to white patients, for the majority of the discussions did not consider the Negro; but the general mildness of streptococcal infections is also applicable to the Negro race. The incidence of such diseases is also less in the warmer climates, and this has led to numerous reports related to the frequency of rheumatic fever in the two regions. Dr. Philip F. Barbour of Louisville, Ky., reported in a personal communication that an examination of some 16,000 children in the Louisville public schools revealed slightly less than one-half of 1 per cent as having any organic heart lesions. It is doubtful that a comparable number of examinations of school children in northern climates could approximate such a low

incidence. That rheumatic heart disease, although relatively infrequent, does occur is borne out by the number of cases seen at the Heart Station of Charity Hospital at New Orleans. From July 1, 1942, to June 30, 1943, there were 28 white females, 52 Negro females, 45 white males, and 42 Negro males with possible and proved rheumatic heart disease. Yet, in a provisional survey at the same institution from Jan. 1, 1942, to Sept. 25, 1944, among 28,562 Negro male children and 44,020 Negro female children examined during that period, there were no diagnoses of chorea.[7] Thus, Sydenham's chorea in typical form must be of rare occurrence in the Negro race.

There is another question to be considered in attempting to explain the more frequent occurrence of chorea in the white child than in the Negro. The problem of nervous stability has often been discussed as a predisposing factor. No one individual is capable of describing the typical Southerner, and characterizations ranging from the dashing hot-blooded cavalier to the phlegmatic, malaria-ridden, hookworm-infested child are familiar to us all. In general though, the less nervous instability of the Negro child as compared with the more pampered white child may be of significance.

Therefore, in summary, Sydenham's chorea, although infrequent in the southern part of the United States, tends to occur less often in the Negro than in the white race. There is suggestive evidence that typical chorea is more severe in the Negro than in the white child, that the pure Negro is less likely to have chorea than the mulatto, and that the stable nervous reactions of the Negro make him less likely to have the disease. Above all, there exists a need for studies of diseases of the Negro, and the most fertile field for such studies lies not in the great hospitals of the South but in the rural communities and must be made by alert general practitioners.

To those busy pediatricians who aided in this survey, I wish to express my sincere appreciation.

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TRACHEOTOMY IN BULBAR POLIOMYELITIS

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FOR the purposes of this paper, acute anterior poliomyelitis may be defined as an acute, infectious, self-limited disease of the central nervous system. Bulbar poliomyelitis is that form of the disease where the infection involves the brain stem and gives rise to clinical impairment of the functioning of any of the cranial nerves. Death in poliomyelitis is usually ascribed to some form of the disease of the bulbar region. Many times the cranial nerves clinically involved are not related to the life or death of the patient. Thus in facial or oculomotor paralysis, when these nerves alone are affected, there is little danger of a fatal outcome. It is when the glossopharyngeal, hypoglossal, and vagus nuclei are involved that the prognosis becomes grave. The degree of weakness or paralysis is, too, of the greatest significance. Thus there may be slight impairment of motion of the palate or there may be complete inability to swallow or phonate. For this discussion these functions must be sufficiently impaired so that there is an accumulation of nasal and buccal secretions.

The mechanism of death in these individuals is sometimes quite mysterious. Evidence of respiratory distress other than obstruction by the accumulated secretions is often present. One frequently finds case reports concluded by the statement that "death was due to respiratory failure." That this failure is due to central rather than peripheral paralysis is evidenced by the fact that the respirations become very slow, irregular, and shallow even though the thoracic excursion appears to be uniform. In other instances death can be traced to central cardiovascular disturbance. Sometimes there is direct evidence of vagal paralysis in a rapid rise of pulse and blood pressure, although this does not appear to account directly for the fatality. In other instances death may be rather sudden and one must hypothesize some form of cardiovascular collapse. These assumptions must necessarily be of a vague nature since the so-called "vital centers" cannot be located with such exactness as to say, "These cells form the nucleus of the vasomotor center." Thus there is no visible affirmation of invasion of the center itself.

In still other cases, extensive pneumonic processes may be present. These result from accumulated secretions in the posterior pharynx, which, with the inability to dispose of them by swallowing or expectorating, are aspirated. Atelectasis and aspiration pneumonia are ever present menaces and are the reasons usually given for the contraindication of the use of the respirator in bulbar poliomyelitis.

The nature of the involvement of the "vital centers" is extremely hypothetical. Some have spoken of edema. However, this does not appear to be

From the Charles S. Wilson Memorial Hospital.

a striking finding at autopsy. It is a matter of common knowledge that the brain is peculiarly susceptible to anoxemia. It would not seem out of reasonable bounds, then, to assume that anoxemia may play a role in the impairment of the "centers." That part of the brain in which the "vital centers" are located is already the site of an acute infectious process. Moreover, there is obstruction to free respiration and there may be atelectasis and pneumonia. For this reason postural drainage has been the method of choice in treating bulbar poliomyelitis. Yet even so, the "vital centers" are all too frequently affected. Thus it happens that the physician would like to put the patient with bulbar poliomyelitis into a respirator for present or impending central respiratory failure. On the other hand he does not dare to do so because of the certainty of aspiration of the accumulated secretions. For this reason some reports have been made on the shunting of the respiratory stream past the "puddled" secretions by means of a tracheotomy.

The next step appears to be a valve mechanism by means of which the inhaled air is shunted past the posterior pharynx with its secretions while the exhaled air forces these secretions farther away from the lungs to where they can be removed by suction or drainage. A tracheotomy tube connected directly to an oxygen system as shown in Fig. 1 has been at least partially successful. It can be seen that it is impossible to exhale through the closed positive

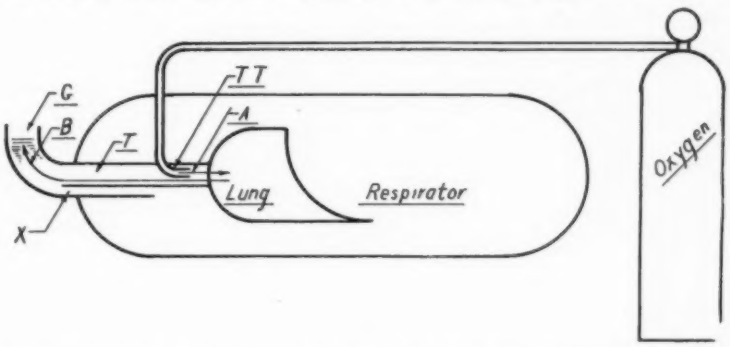

Fig. 1.—Diagram of respiratory valve. *A*, path of inhaled air; *B*, path of exhaled air; *C*, posterior pharynx with accumulated secretions; *T*, trachea; *TT*, tracheotomy tube; *X*, functionally obstructed esophagus.

pressure oxygen system. During the expiratory phase the gases must escape around the tracheotomy tube and out through the nasal pharynx. During inspiration the supply tends to be derived from the oxygen supply system since it is under postive pressure. This is only a tendency, since to deliver a sufficient volume of oxygen to supply all of the tidal air during the inspiratory phase might result in building up too much pressure during the expiratory phase, or even to make it impossible to exhale at all. Thus with the tidal air averaging about 300 c.c., the oxygen set to deliver 6 liters per minute, and the respirator running at 20 respirations per minute, about one-half of the tidal air would be supplied through the tracheotomy tube.

To provide an adequate airway, the tracheotomy tube was altered slightly by soldering a nipple to the inside tube. This allowed the oxygen supply tube to be connected directly to the tracheotomy tube without loss of effective airway. The accompanying diagram (Fig. 2) is self-explanatory.

Two patients with the severe form of bulbar poliomyelitis were treated by this system. Brief reviews of their clinical histories are as follows:

CASE 1.—J. B., 9-year-old, white male, entered the hospital on the service of Dr. Marian S. Morse. On Nov. 12, 1944, he had developed fever, headache, and vomiting. This progressed until November 14, he was unable to swallow and even regurgitated liquids through his nose and mouth immediately after attempting to swallow. On November 15, he was brought to the hospital. Examination revealed an acutely ill, slightly cyanotic, white male with obvious respiratory distress. There were loud, moist râles over the entire chest and a "gurgling" type of respiration. The posterior pharynx was filled with secretion and the palate failed to move. There was slight stiffness of the neck and back. Examination of the spinal fluid showed a cell count of 71 cells per cubic millimeter with 71 per cent polymorphonuclears and 29 per cent lymphocytes. Postural drainage was instituted with some relief. Tracheotomy was done on the afternoon of admission and the patient was placed in the respirator. The next day the chest was clear although there was little respiratory motion out of the respirator. There was left lateral rectus paralysis and the patient was comatose. These were thought to indicate extension of the infectious process to other areas of the brain. His fever had risen to 104.8° F. and penicillin was started. On November 19, an attempt was made to pass a Levine tube but even by direct digital manipulation of the tube it could not be passed into the esophagus. On November 26, respiratory excursions even in the respirator became very shallow and the patient was cyanotic. The trachea was aspirated through the tracheotomy and a moderate amount of tenacious yellow secretion was obtained. Respiratory excursion was again good and the patient was removed from the respirator although the valve mechanism was maintained for about twelve hours thereafter, when he was placed in an oxygen tent in the shock position. On November 29, the Levine tube was finally passed and feedings were given through it. By December 9, the tube feedings were discontinued and from that date recovery has been uneventful. Six months later there is still a slight sticking of solid food and a nasal quality to the voice. Roentgenograms taken at regular intervals have shown no significant degree of atelectasis or pneumonia. He was discharged on Feb. 25, 1945.

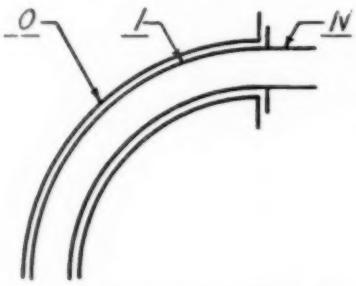

Fig. 2.—Tracheotomy tube used with respiratory valve. *N*, nipple used for direct attachment of oxygen; *I*, inner tube; *O*, outer tube.

CASE 2.—L. B., 13-year-old white male, entered the hospital on Nov. 24, 1944, on the service of Dr. E. M. Jones. He had had a headache for twenty-four hours prior to admission and on the afternoon of admission complained of difficulty in swallowing. A brother had entered the hospital several days earlier with acute anterior poliomyelitis. Physical

examination revealed an acutely ill, white male with slight weakness of both legs on flexion. There were no other signs of disease. The spinal fluid showed a cell count of 37, polymorphonuclears, 24 per cent, lymphocytes 76 per cent. The next morning the patient had a "gurgling" type of respiration. There was a puddle of yellow mucoid material in the posterior pharynx. The palate moved slightly to the left. The larynx did not rise upon attempts to swallow, which resulted in regurgitation through nose and mouth. Tracheotomy was done on the afternoon of November 25, at which time the right pupil was observed to be twice the size of the left. On November 27, the tracheotomy tube was dislodged and after several hours, during which time the patient was in the respirator without the benefit of the valve mechanism, it was replaced. That evening the temperature rose to 104.2° F. after having been below 103° F. for two days. There was slight dullness in the right chest and many coarse râles over the entire chest. Respirations were shallow and slow but because of fluid below the level of the tracheal wound the patient was removed from the respirator. On December 1, the patient became comatose with respirations of from 4 to 8 per minute. He was replaced in the respirator with periodic suctioning through the tracheotomy tube. On one occasion during that day he became pulseless and remained so for an estimated five minutes following the suctioning. His color was good while in the respirator. However, on December 2, cardiac activity suddenly ceased. On autopsy the heart was found to be markedly distended on the right with complete collapse of the left side. The right lower lobe was completely atelectatic. There were patches of atelectasis posteriorly in both lobes of the left lung. There was bloody mucus in the bronchi. Microscopic sections of the brain and spinal cord confirmed the diagnosis of polioencephalomyelitis. The cause of death was thought to be central cardiovascular collapse.

TABLE I

NAME	AGE	SEVERE OR MILD	NERVES INVOLVED	ONSET TO APPEARANCE OF BULBAR SYMPTOMS	DURATION OF BULBAR SYMPTOMS	USE OF VALVE	OUTCOME OF PARALYSIS	AUTOPSY
R. W.	12	severe	9, 10, 11; bilateral	2 days	24 hours	no	fatal (cardiac)	Acute broncopneumonia; acute poliomyelitis
M. Y.	29	mild	left sixth	1 day	persists	no	improved	—
C. K.	13	severe	right 10, 11	3 days	9 hours	no	fatal (cardiac)	Not done
B. R.	10	mild	left third	5 days	persists	no	improved	—
W. O.	22	severe	bilateral; 11	10 days	24 hours	no	fatal	Not done
E. S.	15	severe	9, 10, 11; bilateral	1 day	48 hours	no	fatal	Acute poliomyelitis; acute bilateral bronchopneumonia
M. S.	21	severe	9, 11; bilateral	2 days	5 days persisted until	no	fatal	Acute poliomyelitis; acute purulent bronchopneumonia
G. S.	2	mild	right 7	1 day	discharged	no	improved	—
J. B.	9	severe	10, 11; bilateral	2 days	persists	yes	improved	—
W. C.	31	severe	11; bilateral	10 days	2 days	no	fatal	Not done
E. D.	11	mild	left 11	3 days	19 days	no	improved	—
L. B.	13	severe	9, 10, 11; bilateral	2 days	9 days	yes	fatal	Acute poliomyelitis; atelectasis

These two cases represent the last two severe cases of bulbar poliomyelitis seen in the season from August to December, 1944. In Table I are listed the cases previously encountered during that season. It will be seen that the severe cases in this epidemic have been uniformly fatal in our experience with-

out the valve mechanism. Since the acute disease is self-limited, it would seem that any means to prolong the life of the patient is worth while since it brings him closer to the termination of the process. This usually is followed by the subsidence of the paralysis seen during the acute phase. By means of this valve mechanism it is hoped that some of those individuals dying of respiratory failure from bulbar poliomyelitis can be benefited.

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CARDIOSPASM IN THE NEWBORN

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UNLESS the term cardiospasm is reserved to describe persistent dysphagia, with roentgenoscopic evidence of obstruction to food at the cardiac end of the esophagus, without organic stenosis, confusion in diagnosis frequently occurs. Many patients with intermittent symptomatic retardation of swallowing have been described as suffering from cardiospasm, when probably spasm of the esophagus or of the cardia would have been a more appropriate diagnosis.

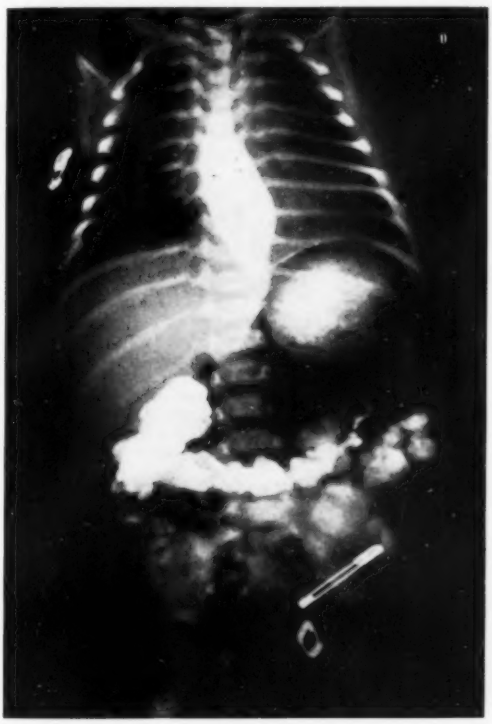

Fig. 1.

Occasional reference is made to the occurrence of cardiospasm at birth, and roentgenoscopic and symptomatic evidence has been presented to substantiate the diagnosis. Relief from symptoms has always followed passage of small catheters through the esophagus, and apparently the belief exists that such treatment dilates the cardia sufficiently to restore normal deglutition. To any-

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one who has had experience in treating patients with true cardiospasm, the beneficial effect of the passage of catheters or of dilators of fairly large size appears doubtful.

The following case is reported in support of this opinion and to suggest that so-called cardiospasm in infancy is the result of temporary incoordination of the nerve-muscle mechanism of swallowing.

CASE REPORT

On March 29, 1942, a baby boy 7 days of age was seen in consultation with his physician. Regurgitation of food had been noted from the time of birth, and roentgenoscopic examination of the esophagus had revealed obstruction to barium at the cardia, with dilation of the esophagus above the point of obstruction (Fig. 1). A diagnosis of cardiospasm had been made. Elixir of nembutal and small doses of atropine had been administered without beneficial results. Because of medication and regurgitation of food and fluid, the child was drowsy and dehydrated. In other respects, the examination disclosed nothing of pathologic significance.

Instead of passing a catheter through the esophagus into the stomach, as had been done in patients previously reported, treatment was limited to concentrated food orally and adequate amounts of fluid subcutaneously. All medication was discontinued. Within a few days regurgitation of food ceased, and the child appeared normal in every way. At a recent examination, three years after the original visit, the patient was well, and roentgenoscopic examination of the esophagus showed it to be normal.

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MENINGITIS CAUSED BY TYPE F HEMOPHILUS INFLUENZAE

Report of a Case With Recovery

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MENINGITIS caused by *Hemophilus influenzae* is an important disease, particularly during infancy and childhood, when its incidence is highest[1, 2] and the mortality is relatively high. In recent years a considerable decrease in the mortality has been obtained by the use of *type-specific antiserum* as developed by Pittman,[3] Alexander,[8] and others. Antiserum was prepared in goats (1911) by Wollstein[4] and the immunological relationships of various strains were studied by Rivers and Kohn,[5] Povitsky and Denny,[6] and by others, but since many of these strains were examined months after isolation, it is quite likely that they had changed from S to R form and had lost their type specificity. Pittman[3] described the encapsulation of the S form of the organism and showed that this form produced a soluble specific substance that precipitated the homologous antiserum. The R form did not possess such specificity.

In 1931, Pittman began preparation of specific antiserum from horses, for the type b form (the type b form was found in 90 per cent of the cultures obtained at that time). This was used in mice with marked success and then administered to patients with varying techniques in eleven clinics, which resulted in few cures, but in a definite reduction of the numbers of bacilli, or in sterilization of the blood stream.[7]

Alexander[8] used a typing technique similar to that of Neufeld's (for the identification of pneumococcal types). She also developed a rabbit antiserum to the therapeutic use of which she credits a decrease of the mortality rate of 92 per cent to a new low of 24 per cent, when combined with sulfonamide therapy.[10]

In Pittman's series of eighteen cases,[7] all but three were caused by the type b organism. One was type a, one was an R variant, and the third was type f. The case caused by type a, showed a sterile blood culture and an improved condition after treatment with type b antiserum, but the patient died four weeks after the antiserum was discontinued. Examination revealed a brain abscess, containing streptococci and staphylococci but no influenzal bacilli. Administration of antiserum in the other two cases (type f, and the R variant) had little effect on the course of the infection.

The present report describes the course of a purulent infection of the meninges, caused by *H. influenzae*, type f. According to Pittman[10] who identified the organism, this was the third type f strain of *H. influenzae* which she has studied. In 1933, Pittman[7] reported the isolation of a type f strain from spinal fluid. Platt[11] reported a few cases of respiratory infections due to the type f organism. Treatment of our case included an intensive course of sulfadiazine. When the temperature continued elevated, he was given a course of penicillin, intra-

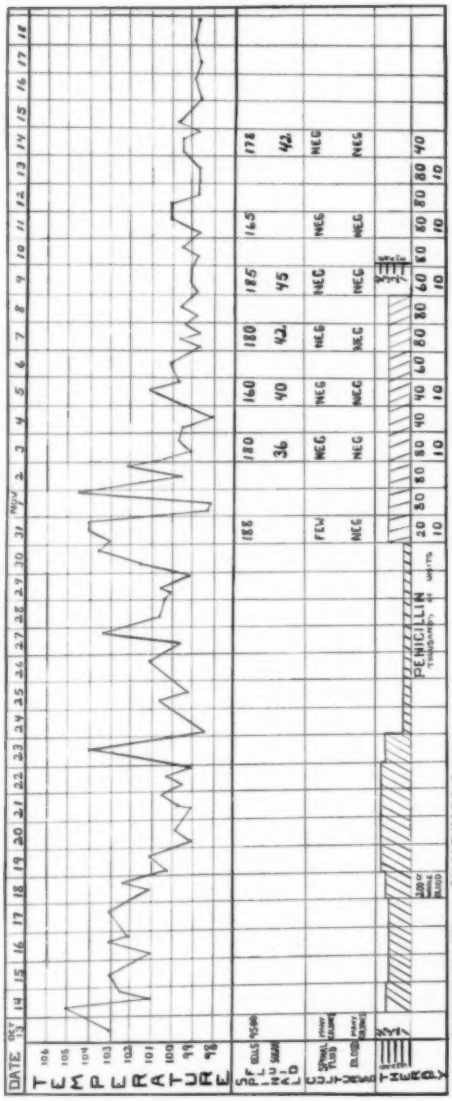
THERAPEUTIC CHART
TEMPERATURE
DATE
SULFADIAZINE
SULFATHIAZOLE
PENICILLIN

Chart I.

thecally and intramuscularly, in conjunction with sulfathiazole. Specific antiserum was not administered.

A 5-year-old white male child was admitted to the contagion ward of Hurley Hospital, Oct. 13, 1944. The onset of his illness was two days prior to his admission, when he began to vomit, became drowsy and irritable, and ran a fever of 102° F. The following day, he refused to lie on his back and drank only water. On the day of admission, he refused to take anything by mouth, became more disoriented, and vomited again.

On admission, he was a thin, well-developed boy, semicomatose, resistant to examination, lying on his side, with the legs and head hyperextended. The temperature varied between 103 to 105° F., respirations were shallow, at the rate of 28 to 35 a minute, and the pulse (125) was regular. The skin was hot and dry, the pupils were very small. Nystagmus was absent. The eardrums were dark but not bulging. The nose and posterior pharynx contained stringy yellowish material, and the pharynx was injected. The neck was very stiff and there were fine, twitching movements of the extremities. The only other abnormal physical finding noted was a bilateral Kernig sign and hyperactive biceps and triceps tendon reflexes on the right. The Babinski sign was normal.

Turbid spinal fluid, under increased pressure, was removed by lumbar puncture. The total cell count was 9,500 cells per cubic millimeter, of which 90 per cent were polymorphonuclear leucocytes and 10 per cent were lymphocytes. There was a 2-plus globulin reaction. A gram-negative bacillus, which failed to show a positive quellung reaction with type b antiserum was observed in the smear, prepared from the sediment.

The admission blood examination revealed a (100 per cent equals 15 Gm. of hemoglobin per 100 c.c. of blood) 98 per cent hemoglobin, 35,000 white cells per cubic millimeter, of which 78 per cent were polymorphonuclear leucocytes, 15 per cent lymphocytes, and 1 per cent monocytes. The urine was clear, having a specific gravity of 1.020. It gave a 2-plus albumin reaction and contained many granular and hyaline casts.

A blood culture yielded a gram-negative rod, later identified as *H. influenzae*, type f, identical with that isolated from the spinal fluid. Dr. Pittman reported: "Morphologically and culturally it was not unlike other type-specific *H. influenzae* cultures. It produced indol, and it gave a positive quellung reaction in type f antiserum."

The patient was immediately treated with sodium sulfadiazine intravenously, and with the usual maintenance doses (3½ Gm. per day) orally. The blood examinations were repeated four, ten, twenty-four, and thirty days after admission. Four days after admission, the white cell count was 20,000 per cubic millimeter, 72 per cent of which were polymorphonuclear leucocytes, 21 per cent lymphocytes, and 7 per cent monocytes. The hemoglobin was 68 per cent and his red cell count was 3.4 million per cubic millimeter at that time. His condition was unimproved and 200 c.c. of whole blood given through a cannula in the saphenous vein was well tolerated. The temperature decreased from 103 to 100° F. during the subsequent twenty-four hours. His neck was much less rigid, and the twitching of the extremities ceased. He continued to be resistant, seemed to be deaf, and within the next few days showed some interest in toys. The temperature was 99 to 100° F. at this time, but the patient did not regain mental alertness. Ten days after admission, the temperature rose to 104°, the white blood cell count to 18,500, with a differential similar to that of six days before; a hemoglobin of 70 per cent and a red cell count of 3.7 million per cubic millimeter. Subsequent urinalysis showed only traces of albumin and only occasional granular casts.

The sulfadiazine blood level was 8.3 mg. per 100 c.c. five days after admission, but since temperature spikes of 104° subsequently occurred on two occasions, the sulfadiazine was discontinued and sulfathiazole and penicillin were administered. The latter was instilled intrathecally as well as intramuscularly. At this time, the spinal fluid contained only 188 white blood cells per cubic millimeter, with a 1-plus globulin reaction and a glucose content of 36 mg. per cent. No bacteria were found on smear, and only a few colonies of the gram-negative bacillus were obtained by culture. At this time there seemed to be some improvement in hearing. The patient recognized his mother, the doctors, and nurses and named the

foods he ate but still appeared to have a mental block. The eardrums were still dark, right more than left, but were not bulging, and the fundoscopic examination was normal.

One spike of the temperature to 104° occurred the day after penicillin and sulfathiazole were administered, but subsequently, the temperature remained between 98 and 100° F.

Penicillin was given intrathecally every two to three days. Although the cell count of the spinal fluid remained at 160 to 175 per cubic millimeter, the globulin dropped to a trace (62 mg. per cent) and the sugar content remained at 42 mg. per cent. Cultures of the spinal fluid made a month after admission remained sterile.

The last blood count made before discharge was 3.9 million red cells per cubic millimeter, 73 per cent hemoglobin and 11,000 white cells per cubic millimeter, 62 per cent being polymorphonuclear leucocytes and 35 per cent lymphocytes.

The patient was discharged thirty-six days after admission, afebrile (four days after discontinuance of all medication), but incontinent, and negativistic. He exhibited periods of uncontrollable laughter, would not talk, smile, or respond to anyone. The prognosis was obviously not favorable, because of the long-continued fever and the apparent deteriorated mental condition.

The patient was seen at his home two months after discharge. The change in his condition was striking. He had gained fifteen pounds, the hearing still seemed to be less acute than normal and his responses were slightly retarded; his attention wandered and he asked to have questions repeated, although it seemed certain that he heard them. He remembered what he had been taught previous to his illness: he could read and write his name, the alphabet, and numbers. His parents noticed that he made new statements and observations.

A complete physical and neurological examination showed only a few things of interest. The optic discs were slightly hazy, but papilledema did not exist. The vessels were slightly tortuous. The right eardrum was still dark, but the landmarks of the left eardrum were present. Auditory acuity was subnormal, and it was not possible to evaluate subjective tests. The Weber test seemed to be referred to his right ear; the Rhinne test was positive on the left, negative on the right, but some unconscious "leading" was possible.

The right thigh was one and one-half inches smaller than his left and the knee jerk was hyperactive on the right. In view of the hyperactive knee jerk, the fact that he had been walking almost a month with no limp suggested the possibility of an organic lesion, rather than disuse. The adductors were weaker on the right than on the left. The remainder of the examination was negative. There has been no evidence of recurrence of the meningitis. An encephalogram in this case would be of interest, particularly in view of the possible existence of organic cortical changes.

DISCUSSION

The significance of this case report is not entirely the fact that the patient recovered from the acute illness, but rather the fact that it represents a case of *H. influenzae* meningitis, caused by an organism other than the usually encountered type b. Obviously such an occurrence is rare but emphasizes the necessity of accurate typing of a given culture before the administration of type-specific sera is contemplated. In this case, antiserum was not given. Recovery of cases of influenzal meningitis as a result of sulfonamide therapy have been reported, but the higher percentage of recoveries have been in those patients who received both a sulfonamide and type-specific antiserum. It is highly probable that the administration of penicillin in this case contributed little to the patient's recovery since it does not ordinarily affect *H. influenzae*. That a beneficial synergistic effect resulted from its administration in combination with the sulfonamides cannot be denied, however.

SUMMARY

The recovery of a case of meningitis caused by type f *H. influenzae* is reported.

Therapy included the administration of sulfadiazine, sulfathiazole, penicillin, and blood transfusion. No type-specific antiserum was used.

Attention is called to the fact that meningitis occasionally may be caused by a type of *H. influenzae* other than type b. Accurate typing of the strain is therefore necessary preliminary to proper specific anti-serum therapy.

I would like to express my thanks to Dr. Pittman for her help in this case and her information concerning the subject; to Dr. E. M. Eichhorn of Flint, Mich., for permission to report this case, and to Dr. W. L. Bradford, of Rochester, N. Y., for his advice in preparing this report.

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THE TREATMENT WITH ANTISERUM OF ACUTE LARYNGITIS CAUSED BY HEMOPHILUS INFLUENZAE

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SINCLAIR[1] first described the syndrome of acute laryngitis and bacteriemia caused by *Hemophilus influenzae* type B. He described ten cases with the constant clinical picture of high fever, shock, acute laryngitis, leucocytosis with predominance of polymorphonuclear cells and positive blood culture. A history of sudden onset was present in each case.

Du Bois and Aldrich[2] described four similar cases, recommending early tracheotomy and adequate sulfonamide therapy.

Pittman[3] demonstrated in 1931 that the invasive strains of *H. influenzae* possess a capsule. In 92 to 95 per cent of cases of influenzal meningitis the organisms have been type B.

We are presenting four additional cases with the same clinical picture. We wish to emphasize the value of the use of *H. influenzae* type B rabbit antiserum in treatment. Sinclair[1] used it in two of his ten cases with good results. In one, however, there had developed signs of meningitis.

Rapid identification of the organism was carried out by the procedure suggested by Alexander and associates.[4] Material was obtained from either the trachea or a bronchus (during bronchoscopic examination) or from direct swab of the nasopharynx. This was typed with *H. influenzae* type B rabbit antiserum.

Alexander[5] concluded that the capacity of sulfonamides to effect complete recovery from type B *H. influenzae* infection is influenced by two factors: (a) the infection must be relatively mild, (b) the drug must be started early in the course of the infection. She believes that only under such conditions will sufficient time be afforded for the patient to produce through his own powers sufficient antibody to overcome the disease.

As indicated by the cases presented and remembering the need for emergency treatment, it would seem advisable to use the antiserum early in the treatment of these cases.

Three of the four patients we are reporting were treated with antiserum. The one who was not treated with antiserum died, in spite of early tracheotomy and sulfadiazine and penicillin therapy in adequate amounts. One patient treated with antiserum was a sibling of the one who died.

Unfortunately, blood cultures were not obtained. However, these cases fit the clinical picture described by Sinclair in all other respects, including positive cultures from nasopharynx or bronchus. Positive capsular swelling for type B *H. influenzae* was demonstrated in the last two cases.

CASE 1.—W. A. A., a 2½-year-old boy, entered the hospital on Jan. 16, 1945.

He was apparently well until about ten hours previous to admission when it was noted that he did not feel well. Four hours later he was found to have temperature of 101° F. About three hours later there was a sudden onset of difficulty in breathing, with

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inspiratory and expiratory stridor. This became progressively worse until admission about three hours later.

Past history was noncontributory.

Physical examination: The patient was an acutely ill child who was very listless and appeared "knocked out" and ashen in color. He had stridor with substernal and suprasternal retraction. There was marked edema of the larynx and pharynx without any membrane present. Except for some suppression of breath sounds throughout, the lungs were clear. Admission temperature was 102.6° F. and it rose to 104° F. in two hours. He was given oxygen and placed in a room for steam inhalation without benefit. His condition was becoming worse and prostration much more marked. About an hour after admission bronchoscopy and tracheotomy were performed. All branches of the bronchial tree that were visualized were "fiery red" and somewhat edematous. Tracheotomy afforded a great deal of relief, although he continued to have moderate substernal retraction.

The laboratory examination showed 27,500 white cells with 91 per cent polymorphonuclear cells. Red cells were 3.4 million. Hemoglobin was 70 per cent. Urinalysis was essentially negative.

Microscopic examination of material from a nasopharyngeal swab disclosed gram-negative diplococci with morphology of *Micrococcus catarrhalis*, but no *H. influenzae*. Culture of material from the trachea, obtained at bronchoscopy, yielded a heavy growth of *H. influenzae*, with some pneumococci, short chain streptococci, and *M. catarrhalis* present. This culture did not grow out, however, until after the patient's death.

After tracheotomy, he was given 30,000 units of penicillin intramuscularly and 20 grains of sodium sulfadiazine intravenously, in addition to intravenous fluids, oxygen, and the steam room. Penicillin, 10,000 units every two hours, and sulfadiazine, 7.7 grains every four hours, were continued.

The patient's respirations became progressively more labored, with marked substernal retraction. Breath sounds bilaterally became progressively more diminished, with definite tubular character.

About six and one-half hours after admission, he was having such great difficulty that bronchoscopy was deemed necessary again, hoping to remove secretions. At bronchoscopy the branches of the bronchial tree remained very red and the edema was markedly increased. The lumen in the right and left main stem bronchi were each practically obliterated by the edema of the mucosa. The smaller bronchi could not be visualized. There was little benefit afforded from this examination.

In spite of aspirin and tepid sponges his temperature remained elevated, never being lower than 101.4°.

The patient became progressively worse and had greater difficulty in breathing. He appeared as though too tired to take another breath all through the day. He was given a transfusion of 100 c.c. of whole blood.

In spite of these measures he expired twenty-three hours after admission. An autopsy could not be obtained.

In retrospect the diagnosis was acute laryngotracheobronchitis produced by *H. influenzae*.

CASE 2.—A. M. A., an 18-month-old male (brother of W. A. A., Case 1), was admitted Jan. 18, 1945 (thirty-six hours after W. A. A. died). There was a history of nasal discharge and cough for about twenty-four hours. He was seen by a local doctor at onset of this illness. Physical examination revealed reddened, congested, nasal mucosa and no other positive findings. Twelve hours later he had some redness of the right eye; the pharynx was red; and parents stated he had "some fever." He awoke from a nap just before admission with a hoarse, croupy cough.

Physical examination: The temperature was 101° F. The pharynx was red and edematous. There was "a croupy cough." The chest was clear. There was no retraction noted. The patient appeared ill and apprehensive.

The laboratory examination showed 4.7 million red cells and 11 Gm. of hemoglobin. There were 16,800 white cells with 49 per cent polymorphonuclear cells. Urinalysis was negative.

Smear of a nasopharyngeal swab showed a predominance of *H. influenzae* with some pneumococci and short chain streptococci.

On admission the patient was placed in a room for steam inhalation and was given sulfadiazine, 7.7 grains every four hours; penicillin, 20,000 units immediately, and 10,000 units every two hours. Fluids were forced.

Within an hour after admission patient began to have both inspiratory and expiratory stridor. He began to present the same clinical appearance that his brother had on admission. The temperature went to 103.4° F. It was decided, because of the brother's clinical course and the presence of *H. influenzae* on smear, to administer rabbit antiserum. Fifty milligrams of *H. influenzae* type B rabbit antiserum in 300 c.c. normal saline was given by slow intravenous drip.

Evidence of laryngeal obstruction became less marked in a short time, although a croupy cough continued during the next twenty-four hours. Almost ten hours after antiserum was started the nurse's notes stated that the "baby was in a playful mood." His temperature rose to 101° the next day but thereafter was not above 100°.

His further course in the hospital was uneventful. The patient was ready for discharge on the sixth hospital day. At this time white cells were 10,950 with 17 per cent polymorphonuclear cells and 77 per cent lymphocytes. Hemoglobin was 13 Gm. He has remained well since discharge.

CASE 3.—H. C., a 3-year-old white male, was perfectly well until fourteen hours before admission when it was noticed that he was having difficulty breathing and felt hot. His respiratory difficulty became progressively worse until admission.

Family and past history was noncontributory.

Physical examination: Temperature was 101° F. He was a very sick, pale, tired, and listless child, struggling for breath, with an inspiratory stridor and marked substernal and suprasternal retraction on inspiration. The pharynx was injected, and coughing produced a thick, tenacious, purulent sputum. Respirations were rapid and noisy and on auscultation there was slight, generalized suppression of breath sounds.

This patient was immediately given steam inhalation. He was given sulfadiazine, 2 grains per pound body weight each twenty-four hours. Penicillin, 10,000 units, was given intramuscularly immediately, followed by 10,000 units intramuscularly every two hours. Two hours after admission, after receipt of the report from the laboratory that *H. influenzae* were seen on smear, he was given 75 mg. of type B *H. influenzae* antiserum in 250 c.c. normal saline intravenously.

The patient was gradually becoming more exhausted and was totally unable to rest because of the respiratory difficulty. Therefore, with the motive of conserving strength and affording relief, elective tracheotomy was done five hours after admission. Bronchoscopy was done at the time of the tracheotomy, and the bronchial mucosa was seen to be inflamed and edematous.

Hydration was maintained by intravenous fluids until the fourth day of hospitalization when the patient began taking fluids well by mouth. His temperature never went above 101° and stabilized at normal on the sixth day of hospitalization.

Recovery was uneventful. The tracheotomy wound was closed on the seventeenth day of hospitalization and the patient was dismissed on the twentieth hospital day.

Laboratory report: On admission there were 6,150 white blood cells, 64 per cent of which were polymorphonuclear leucocytes, 34 per cent lymphocytes, 1 per cent monocytes, and 1 per cent eosinophiles. The red blood cell count was 4,510,000 with 11.5 Gm. hemoglobin. Urine was essentially negative. A throat smear revealed pneumococci, *M. catarrhalis*, and many small gram-negative diplobacilli with the morphology of *H. influenzae*. These same organisms grew out on culture with *H. influenzae* the predominating organism. Some of these gram-negative diplobacilli showed positive capsular swelling with type B *H. influenzae* rabbit antiserum. A culture taken from the trachea at time of tracheotomy gave identical results. The white blood cell count was repeated on the fourth day of hospitalization at which time it was 10,000.

CASE 4.—S. C., an 11-month-old child, was admitted at 12:30 P.M. on April 25, 1945. On the day prior to admission, it was noticed that he had a cold, slight fever, and was somewhat irritable. However, at bedtime he seemed much improved, went to sleep easily, and slept well until 12 o'clock midnight when he awoke with a croupy cough and was struggling for breath. As this continued, he was brought to the hospital twelve hours after onset.

Past and family history was noncontributory.

Physical examination: The patient was a very acutely ill, listless, somewhat cyanotic child with a temperature of 103.2° F. Respirations were very difficult with marked inspiratory stridor and sternal retraction. Throat was injected, and coughing produced a thick, purulent, tenacious sputum which was sent to the laboratory for smear and culture. Coarse rhonchi were heard over the trachea, but no râles were heard in the lungs. Auscultation was very unsatisfactory because of the inspiratory crow.

This patient was given steam inhalation initially, but he was changed to an oxygen tent three hours later on the advice of the nose and throat staff. He was given sulfadiazine, 2½ grains per pound body weight each twenty-four hours, and penicillin, 10,000 units immediately and 5,000 units every two hours thereafter. On receipt of the report from the laboratory that numerous *H. influenzae* organisms were seen on smear with very few other organisms, 50 mg. of type B *H. influenzae* rabbit antiserum were given in 250 c.c. of normal saline intravenously.

This patient was watched closely for signs of fatigue, indicating the need of tracheotomy. However, marked clinical improvement was seen within a few hours after medication was begun. Therefore, tracheotomy was not done. The temperature dropped rapidly to normal within eight hours after the antiserum was administered and remained normal thereafter.

Recovery was rapid and uneventful and the patient was discharged May 3, 1945, on the tenth day of hospitalization.

Laboratory report: The admission white cell count was 16,500, 59 per cent of which were polymorphonuclear cells, 33 per cent lymphocytes, 6 per cent monocytes, and 2 per cent eosinophiles. The red cell count was 3,620,000 with 11.9 Gm. hemoglobin. Urine was negative. Throat smear showed numerous gram-negative diplobacilli with very few other organisms. Throat culture showed a predominance of gram-negative diplobacilli which were recognized as *H. influenzae* and which showed positive capsular swelling with *H. influenzae* type B rabbit antiserum. A few colonies of pneumococci and staphylococci also grew.

DISCUSSION

It would seem that in these cases of influenzal laryngitis, the best results can be expected with the use of type B antiserum in addition to sulfonamides and penicillin. Apparently, the use of antiserum is lifesaving in some cases. It probably prevents the necessity of tracheotomy in some cases if used early.

The response to prompt treatment with antiserum has been dramatic. The emergency nature of these cases has been emphasized.

SUMMARY

1. Four cases of acute influenzal laryngitis have been presented. Two of these were demonstrated to be type B.

2. The first patient, treated with only sulfadiazine and penicillin, died; the other three, given *H. influenzae* type B rabbit antiserum, made rapid, uneventful recoveries.

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MENINGOCOCCIC MENINGITIS

A Report of Multiple Cases Occurring in the Same Family

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MULTIPLE cases of meningococcic meningitis in the same family are known to be infrequent. Holt and MacIntosh state "in 70 per cent of the cases investigated in the New York epidemic of 1904-1905, but one person in the household was affected, while in the sporadic form from 1910-1925, more than one case was reported in only 3 per cent of the families."

In a review of the literature, Hoyne and McEnery[2] reported three cases in one family occurring over a period of sixteen days. They stated that Boldun and Goodwin reported fifteen hundred cases with only eighty-eight instances of more than one case in the same family and that Josephine Neal reported five hundred cases in thirteen years with familial incidence noted but thirteen times. They cited knowledge of two cases and four cases occurring, respectively, in each of two families. Gilmore and Ashworth[3] reported two fulminating cases in the same family.

During the Louisville epidemic in the winter of 1943-1944, three siblings with meningococcic meningitis were admitted to the Isolation Ward of the Louisville General Hospital within a period of thirty-six hours. The following cases are reported:

Case 1.—J. B., 11-month-old Negro twin female, was admitted from the Pediatric Clinic to the Isolation Ward on Jan. 21, 1944. Onset of the illness had been less than twenty-four hours prior to admission with vomiting and high fever. Convulsive movements were noted by the mother twelve hours later. The past history was essentially negative with the exception of one month's hospitalization for nonspecific diarrhea at 6 months of age. Family history showed the parents to be in apparently good health and the four siblings to have minor colds.

Physical examination presented an acutely ill infant with a temperature of 103.5° F., a pulse rate of 140 per minute, and a respiratory rate of 35 per minute. The skin was hot and dehydrated. Both lung fields were filled with fine moist râles. The heart was rapid and heart sounds were feeble. The fontanel was bulging and tense. Nuchal, Kernig, and neck and contralateral Brudzinski signs were positive.

The spinal fluid was markedly turbid with 7,070 white blood cells (predominantly polymorphonuclear leucocytes) per cubic millimeter and gave a positive Pandy test for globulin. The sugar content was 45.5 mg. per cent and the total protein 200 mg. per cent. On culture, meningococci type 1 were isolated.

The hospital course was rapidly downhill, the patient expiring three and one-half hours after the administration of intravenous sodium sulfapyridine and supportive and emergency measures.

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At necropsy the pathologic findings were limited to the lungs and central nervous system. The upper portion of the right lower lobe of the lung was firm, indurated, and reddish brown in color. The subarachnoid space of the brain, especially the sulci, contained a yellowish gray purulent material. The meninges were uniformly clouded with a fibrinopurulent exudate and there were many petechiae and ecchymoses. Cross sections revealed marked congestion, petechiae and encroachment on the ventricles due to edema. Pathologic diagnosis was meningococcic meningitis and bronchopneumonia.

CASE 2.—About twenty-one hours after admission of J. B. her 2-year-old sister, N. B., was admitted to the Isolation Ward with a history of illness of only three hours' duration. Onset was explosive with convulsions and fever occurring simultaneously and followed by marked irritability. The past and developmental history was noncontributory.

Physical examination presented an acutely ill, irritable, 2-year-old Negro female child with a temperature of 103.0° F., pulse rate of 120 per minute, and a respiratory rate of 22 per minute. Petechiae appeared over the chest, back, abdomen, and extremities during the examination. Nuchal, Kernig, and neck and contralateral Brudzinski signs were positive.

Spinal fluid examination revealed a white cell count of 391 per cubic millimeter (predominantly polymorphonuclear leucocytes) and a positive Pandy test for globulin. Sugar content was 66 mg. per cent and the smear revealed gram-negative diplococci which on culture were proved to be meningococci (type 1). The red blood cell count was 3,760,000, the white cell count 34,950 with 79 per cent polymorphonuclear leucocytes. Blood Kahn test was negative.

Treatment consisted initially of 2 Gm. of sodium sulfadiazine and 30,000 units of polyvalent meningococcic antitoxin intravenously. This was followed by 1 Gm. each of sulfadiazine and sodium bicarbonate orally every four hours for thirty-six hours, then ½ Gm. of each every four hours for five days. The patient also received calcium chloride, 1 Gm. four times daily; vitamin K, 4 mg. daily; cevitamic acid, 50 mg. daily, and blood transfusions.

The hospital course was uneventful with complete recovery.

CASE 3.—G. B., 11-month-old fraternal twin of J. B., was admitted thirty-six hours after the admission of the latter to the Isolation Ward with a complaint of a stiff neck which had first been noticed that morning. The infant had a history of a cold which became worse the day before admission but no other symptoms had been noticed. Past and developmental history was essentially negative with the exception of a one-month period of hospitalization for nonspecific diarrhea at 5 months of age.

Physical examination revealed an acutely ill male infant with a temperature of 106° F., pulse rate of 130 per minute, and a respiratory rate of 24 per minute. The infant lay in opisthotonos and the fontanel was bulging. Nuchal, Kernig, and neck and contralateral Brudzinski signs were positive.

The spinal fluid was under increased pressure and cloudy. Examination revealed white cell count of 13,000 per cubic millimeter (predominantly polymorphonuclear leucocytes). Sugar content was below 40 mg. per cent; protein, 100 mg. per cent; chlorides, 413 mg. per cent. Smear showed gram-negative diplococci which on culture were proved to be meningococci (type 1). The red blood cell count was 2,870,000; the white cell count 14,850 with 54 per cent polymorphonuclear leucocytes.

Treatment consisted initially of 2 Gm. of sodium sulfadiazine intravenously followed by 1 Gm. each of sulfadiazine and sodium bicarbonate orally every six hours for thirty-six hours, then 0.5 Gm. of each every six hours for five days. Other therapy consisted of vitamins C, D, and K, calcium lactate, and blood transfusions.

The temperature was normal in twenty-four hours and an uneventful recovery was made.

SUMMARY

We here add to the literature a report of three cases of meningococcic meningitis in the same family. It is interesting to note that the three cases

were hospitalized within a period of thirty-six hours; one case terminated fatally within three and one-half hours following admission. In order to avoid multiple cases in the same family it may be wise to give all members of the family of any patient with meningococcic meningitis a day's supply of sulfadiazine. It is known that from 1 to 2 Gm. per day converts a throat culture from positive to negative.

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CYSTIC TUBERCULOSIS OF THE BONE IN A CASE OF MILIARY TUBERCULOSIS

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CYSTIC tuberculosis of the bone is a condition comparatively rare in pediatrics. The present case is of particular interest in that tubercle bacilli were demonstrated by direct smear in pus aspirated from the lesion and because of the unusual x-ray appearance of the bone.

CASE HISTORY

R. L. R., a white male infant, 2 years of age, was admitted to St. Louis Children's Hospital on Jan. 21, 1945, with a history of intermittent otorrhea for six months; cough, vomiting, and listlessness for two weeks; and cervical rigidity for twelve hours. About six months prior to admission, the mother first noticed pus draining from the left ear. Despite therapy, the otorrhea persisted. This did not seem to interfere with his general health, however, since the child was active, ate well, slept well, and played in a normal manner. About two weeks before admission, he began to cough and vomit. The mother attributed these symptoms to an upper respiratory infection. Vomiting usually occurred after a coughing spell, about three times daily. Vomiting was partially controlled by a liquid diet, but gradually the patient became more ill with increasing listlessness and anorexia. Twelve hours prior to the child's admission, his neck was noted to be stiff.

Past history was interesting in that the baby was thought to be sensitive to eggs and "sweets" and would wheeze after eating them. Since the age of 6 months, the infant had been drinking unpasteurized milk. There was no family history of tuberculosis and no history of contact with any tuberculous person.

On admission, physical examination revealed a well-developed and moderately well-nourished infant, who was extremely listless and reacted very little even to intense stimuli. Temperature was 38.4° C. Respiration was markedly depressed with frequent apneic pauses. The skin was pale. Tissue turgor was poor. When the infant was disturbed, jerking movements of the right side of his body were observed. Bilateral choking of the discs was seen on ophthalmoscopic examination. Both external recti were paralyzed. Facial paresis of the central type was present, more marked on the left side. Cracked-pot resonance was elicited on percussing the skull. The right eardrum was gray and thickened, the left ear canal filled with pus. There was no generalized lymphadenopathy, but cervical lymph nodes were enlarged slightly. The nuchal rigidity was definite. The lungs were clear except for occasional rhonchi. The tip of the spleen was palpable. The knee and ankle jerks were exaggerated, and Babinski's sign was present bilaterally. No clonus was present. The abdominal reflexes could not be elicited. Brudzinski's and Kernig's signs were positive. The left arm and leg were paralyzed. No gross deformity of the extremities was detected on external examination.

LABORATORY FINDINGS

Blood: red blood count 4,140,000; hemoglobin 10.0 Gm. per cent; white blood cells 12,650; platelets plentiful; red blood cells, hypochromic; differential count: stab cells, 2 per cent, segmented cells 69 per cent, lymphocytes, 23 per cent; and monocytes, 6 per cent. Urinalysis revealed nothing abnormal. Culture of pus from the left ear gave abundant growth of *Staphylococcus aureus*. Cerebrospinal fluid: clear; no "web" formation; 165 cells, 93 per cent lymphocytes; Pandy, 4 plus; no organisms seen on direct smear; no growth

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on the chorioallantoic membrane of embryonated hen's eggs, none on blood agar; spinal fluid sugar, 9.5 mg. per cent with simultaneous blood sugar level of 95.5 mg. per cent. The tuberculin test (0.1 mg. O.T.) was positive. The blood Kahn was negative.

ROENTGENOGRAPHIC FINDINGS

Skull (Report, Jan. 22, 1945). "The lateral side to the film: The skull is symmetrical; the sella is within normal limits; there is some separation of sutures, most marked in the coronal sutures. The anterior fontanel is not closed. X-ray diagnosis: Increased intracranial pressure."

Chest (Report, Jan. 24, 1945). "A-P view of the chest, supine: There is a generalized increase of the hilar shadow on both sides, particularly on the right. There is generalized thickening of the bronchial branches and fine parenchymatous mottling scattered throughout both lungs."

Right lower extremity (Report, Jan. 24, 1945). "The proximal epiphysis of the tibia has a rarefied area in its lateral half. The rarefied area is enclosed by a zone of compact bone. Similar areas involve practically all of the tuberosity of the tibia and extend backward halfway through the bone. X-ray diagnosis: Xanthomatosis."

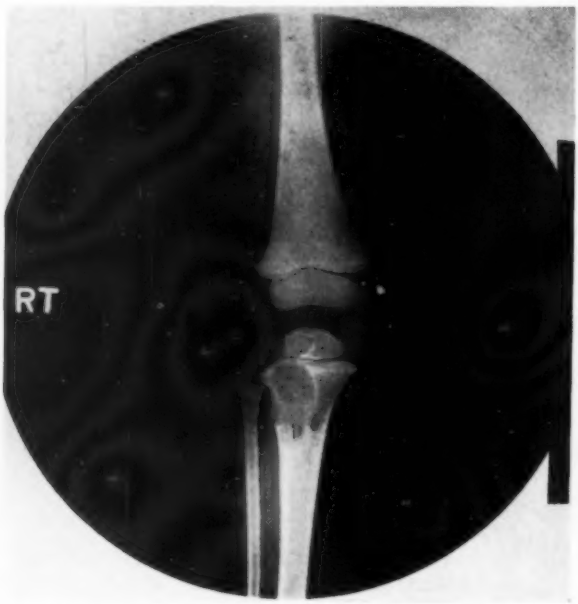

Fig. 1.—Roentgenogram of the right tibia, anteroposterior view.

COURSE IN THE HOSPITAL

Diagnostic impressions at the time of admission included tuberculous meningitis, encephalitis, and brain abscess. Involvement of the skeletal system was not suspected on admission. Since brain abscess was kept in mind as a possibility, penicillin therapy was given intrathecally and subcutaneously immediately after entry. Parenteral fluids included subcutaneous sodium sulfadiazine in the dosage of 0.4 Gm. per kilogram of body weight per day. Penicillin and sulfadiazine were discontinued after diagnosis of tuberculosis was established.

When routine fluoroscopy was performed, all the bones appeared normal except the right tibia which had a defect at the site of the tuberosity. Careful palpation of the region over

the tuberosity of the right tibia revealed an area of softness at the site of the bony defect. An x-ray film of the tibia was taken on January 24 (vide supra). With the aid of the roentgenogram, aspiration was attempted, and 4 c.c. of thick white pus admixed with a small amount of blood were removed. Direct smear of the aspirated material revealed numerous acid-fast bacilli, many in clumps. Subsequently, a guinea pig inoculated on January 25 with this material failed to grow normally and appeared ill. On March 14, the guinea pig was sacrificed and examined. Grossly, there was evidence of tuberculosis in the liver and the peritoneum; direct smears showed the presence of numerous acid-fast bacilli.

The patient expired on the eighth hospital day. The clinical course together with the spinal fluid findings, positive tuberculin test, and demonstration of acid-fast organisms in aspirated pus, made the diagnosis of tuberculous meningitis and tuberculous osteitis definite.

The autopsy findings of the patient showed evidence—grossly and microscopically—of acute miliary tuberculosis of the lungs, liver, spleen, and leptomeninges. The proximal portion of the right tibia was explored, and a fragment of necrotic bone was removed. Microscopic section of this piece of bone showed typical tuberculous involvement. Special staining methods, however, failed to reveal the presence of acid-fast organisms.

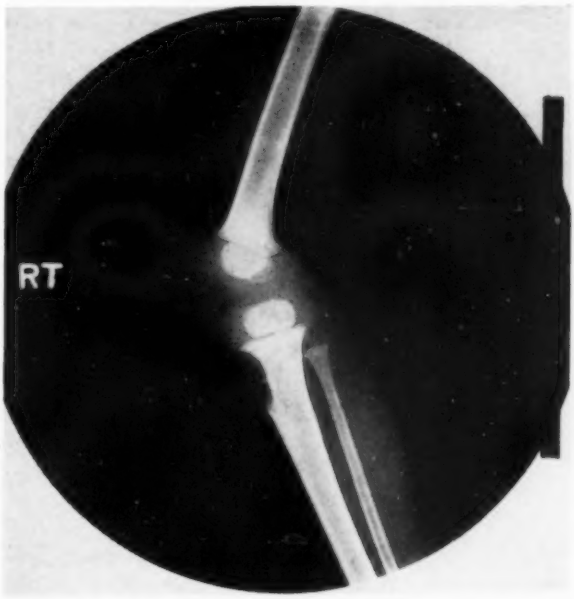

Fig. 2.—Roentgenogram of the right tibia, lateral view.

DISCUSSION

Cystic tuberculosis of the long bones is a comparatively rare condition especially in infants or very young children. Schwentker,[1] in 1931, reported the first case in this country. He pointed out that tuberculous processes in the long bones of children may be divided into two groups according to location, those in the diaphysis and those in the metaphyso-epiphyseal region. He stressed the fact that if the lesion is at the metaphyso-epiphyseal region, a cystic structure results; whereas, if in the diaphysis, the lesion is modified by

periosteal reaction. Petter and Medelman[2] found only eight cases (seven adults and one infant) of tuberculosis of shafts of the long bones in a series of 4,894 general admissions to a sanatorium for tuberculous patients.

Where multiple cystic areas are observed, the question of osteitis tuberculosa multiplex cystoides, as reported by Jüngling,[3] and multiple cystic tuberculosis of the long bones must be considered. Some authors[4] have concluded that these conditions are identical, while others[5] separate them, classifying osteitis tuberculosa multiplex cystoides as a type of sarcoid unrelated to tuberculosis and multiple cystic tuberculosis of the long bones as tuberculous in etiology. The evidence as presented in the literature seems to favor the latter view.

In our patient the lesion was confined to a single bone, the tibia, with involvement of both the metaphysis and the epiphysis. There was no gross deformity of the extremity, and x-ray appearance of the bone was definitely cystic. There were no periosteal changes and practically no local tissue reaction to the infection. Poor resistance in this patient may have accounted for the lack of reaction of the bone to infection and for the presence of large numbers of bacilli in the pus aspirated from the lesion. This case is also unusual from the x-ray point of view (Figs. 1 and 2). There was no swelling of the subcutaneous tissue and no sign of periosteal reaction. The knee joint was not involved. The bony defect was filled out by caseous material which, being less radiopaque, gave the lesion a cystoid appearance on anteroposterior view, a punched-out appearance on lateral view. There was no evidence of bony regeneration or sequestral formation.

While other osseous lesions must be considered, such as syphilis, osteomyelitis, xanthomatosis, the differential diagnosis in this case presented no real problem because of the clinical picture and the ease with which tubercle bacilli were demonstrated.

It is worthy of emphasis that routine fluoroscopy of the skeleton[6] revealed the presence of a bony lesion which was not suspected on routine physical examination. Even after the location of the lesion was known, local signs were minimal. Softness was detected only by careful palpation.

SUMMARY

Cystic tuberculosis of the metaphysis and epiphysis of the tibia is described in a 2-year-old child with miliary tuberculosis. The x-ray appearance of the osseous lesion is unusual. Ante-mortem diagnosis of the bony defect was made by the demonstration of tubercle bacilli on direct smear of material aspirated from the bone. Inoculation of this aspirated material into two guinea pigs produced tuberculosis.

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ARACHNODACTYLY—UNUSUAL COMPLICATION FOLLOWING SKULL INJURY

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IT WOULD appear that interest in this unusual clinical syndrome had been stimulated by the report of Green and Emerson[1] in 1943. Several more reports now appear in the literature which reveal unusual features of the disease first reported in 1896 by the late Dr. Marfan. Stern[2] and Deutch[3] have given particular consideration to the striking ocular defects. There has not been any recent contributions which would refute the increasingly considered theory that the multiple defects arise from an abnormality of the mesoblast. Toward the usage of the name "congenital mesoblastic defect" Haridas[4] points out "with the exception of the eyes, only mesoblastic tissues are involved." A realm for further investigation is suggested by Rones[5] who has recently pointed out the relationship of rubella during early pregnancy and congenital defects in babies. Such defects include cataracts, deaf-mutism, heart disease, microcephaly, and mental retardation. Our primary interest should be directed toward understanding the etiology of these anomalies and developing preventive measures to reduce the occurrence of such social misfits.

CLINICAL FEATURES

The clinical features of these cases are clearly described by Baer.[6] The increased length of the bones of the hands, feet, and extremities is a suggestive clue to the diagnosis. The "spider hands and feet" are impressive of the frailty of the other body structures. The x-rays reveal the rarefaction and spindly appearance of the bones of the hands and feet. Because of the length of the feet and relaxation of the ligaments, pes planus is common. The over-all length may be increased but spinal abnormalities may alter this total measurement. The gross appearance of frailness is enhanced by the atrophy of muscles and deficiency in subcutaneous fat. Greater joint mobility is produced by relaxation of the ligaments. The muscle atrophy may give rise to limitation of activity due to increasing contracture.

The funnel-shaped chest and thinness of the chest wall are well illustrated by the photographs of the Chinese child described by Haridas. The usually associated precordial bulge* is not revealed in his case, but there are congenital heart defects in 30 per cent of these cases. Mild clubbing of the fingers was noted in the case described here. Abnormalities of the lungs may be found in the form of absence of one lobe or a small right middle lobe.

The multiple ocular defects make the eyes important in making the diagnosis and in affecting the patient's total life adjustment. Baer reported that

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*See photographs of chest deformity with precordial bulge and characteristic hands and feet in clinical report by Green and Emerson.[1]

bilateral abnormalities occur in over 50 per cent of the cases. Pasachoff, Madonick, and Drayer[7] state that the commonest anomaly is the bilateral dislocation of the lenses associated with tremulous irises in 62 per cent of the cases. Myopia, shallowness of the anterior chamber, miosis, and strabismus are also found. In 1942 Rados[8] reviewed the 204 reported cases of Marfan's syndrome and discussed ten cases of subluxation of the lens in which seven had unmistakable signs of arachnodactyly. Dax[9] draws attention to an interesting correlation between Marfan's syndrome and Laurence-Moon-Biedl syndrome. He reports four cases of arachnodactyly in which retinitis pigmentosa was found in two and cerebro-retinal degeneration in one. The suggested relationship between dienecphalic disturbances and retinitis pigmentosa has already been discussed by Zondek and Koehler. Pause regarded the Laurence-Moon-Biedl syndrome essentially due to involvement of the hypothalamus with degenerative changes. Dax concludes that it is "not surprising to find arachnodactyly associated with retinitis pigmentosa or juvenile amaurotic idiocy, or that four cases of ectopia lentis have been recorded in connection with retinitis pigmentosa."

Recent reports bring out more diffuse abnormalities than discussed by Baer. He states that "other viscera, ductless glands, nervous system, blood vessels, skin, sex organs and secondary sex characteristics are usually normal." Dax states there is usually a retardation of sexual development and undescended testes have been noted. He further emphasizes that "the relationship to oligophrenia has never been stressed." This oligophrenia (the *amentias* of the British literature and the *oligergastric reaction sets* of Meyerian terminology) is well illustrated in Dax's cases in which three patients are idiots and one a feebleminded deaf-mute. Pasachoff[7] has also reported the studies of the intelligence levels of three of the four siblings in his report. The two children with typical arachnodactyly had intelligence quotients of 73 and 55; the 4-year-old girl operated on for a cataract, later developing bilateral iridodonesis, was stated as having "average intelligence."

CASE REPORT

D. M. (Case No. CP-1180) was a 13½-year-old adolescent female admitted to the Psychiatric Service for diagnosis and recommendations regarding school placement. The referring Board of Education was anxious to know whether she possessed any capacity for special training or should be excluded from the public school system.

Family History.—The 49-year-old father was a rather simple, opinionated man with eighth grade education. He gave the original history as his wife was "too afraid to talk to the doctor!!" She was seen to be a small-headed, not overly clean or intelligent, 44-year-old woman. There were seven siblings aged from 22 to 5 years; all apparently had normal intelligence save the 7-year-old boy who had not yet started school. Mental diseases and congenital anomalies were denied in the familial history.

Past History.—Pregnancy was uneventful. The birth weight of 8½ to 9 pounds was average as compared with the siblings. The delivery in a local hospital was easy. The parents emphatically denied that any abnormality had been noted by the family doctor at time of birth. She was said to be "just as strong and normal as the rest of the children" until two years of age.

Suggestion of developmental retardation was evidenced by the delay of walking and speech formation until 24 months. One doctor put braces on the child's legs at 24 months;

by 30 months she was walking some. At 4 years another doctor took x-rays of the hips and pelvis and found a fracture of the neck of the left femur and placed the girl in a cast for several months. At about 4 years the mother noted "she would look out of the corners of her eyes." At 6 years she was not accepted at parochial school because the Sister said the girl was unable to see. Several oculists were consulted but advised against glasses or operative interference.

Present Illness.—A reconstruction of the history from the time of exclusion from school until the present study at 13½ years reveals clearly a progressive failing of vision. One oculist told the parents when the girl was 6½ years old that he could not put on glasses "until she could read and write." She remained at home playing as much as she could with her younger siblings. About all she could do around the home was to help with the dishes. Vision was too poor even to bathe herself successfully. For a while she could still recognize faces; gradually she bumped into things more and more. At the time of study the mother said that the patient "could not tell the difference between day and night."

In the summer of 1943 she was playing outside in the yard. Attempting to find her playmates during a game she fell down the open cellar door. Sometime later the mother found her unconscious down in the cellar. How long she had been there was unknown. Cuts about the arms, legs, and eyes were seen. For two weeks she was kept in bed. Symptoms of concussion could not be elicited from the parents. D. M. did complain about her "eye bothering her" and within two to three weeks the left eye was becoming prominent. The appearance of this eye at the time of examination is shown in Fig. 1. After other oculists had examined the girl and given varied opinions about operations and prognosis, the parents requested help from the local Board of Education in determining whether there would be any possibility for special class training and assessing of the total psychobiological make-up.

Fig. 1.—D. M., showing exophthalmos, exophoria, and dense fibrous bands in left eye with arrested glaucoma.

Hospital Findings.—D. M. was an amiable, not unpleasant or uncooperative girl. She endeavored to do as much for herself on the ward as her visual and mental incapacity would allow. Her nutritional state was good as revealed by the weight of 40.0 kilograms and height of 146.2 centimeters. On the Wetzel Grid her position was in the M channel at the 115 level and retarded 6 months on the auxodrome. The standing height was decreased because she stood on the shorter left leg which still showed shortening of the femur neck by x-ray. The length of the left leg was 7.1 centimeters less than the right leg. The span was 148.2 centimeters; again somewhat decreased because of the semiflexion of the arms at the elbows due to tissue and muscle contracture. The decreased subcutaneous tissue of the lower extremities was pronounced. The lower measurement was 81.2 centimeters. Fig. 2 reveals the spinal column defect which was well illustrated in the x-ray of the pelvis by a marked upward

tilting of the left side. The "spider hands and feet" were typically those seen in other illustrations of this syndrome. The x-rays of the hands, Fig. 3, show clearly the frailty of the osseous elements with tapering toward the distal ends of the metacarpals and some rarefaction of the distal ends of these bones. The head measured 55.0 centimeters in occipitofrontal circumference; dolichocephaly and prognathism were not present; the skull x-ray did reveal an unusual thickness of the calvarium and a slight osteoporosis.

Fig. 2.—D. M., showing shortening of left leg and associated scoliosis; pes planus; gauntness of extremities with early elbow contracture.

The exophthalmos and exophoria of the left eye gave an arresting facial appearance. Both lids could be closed and there was no lid lag. The greater dilation of the left pupil can be seen in Fig. 1, as can the fibrous bands in the vitreous. The consultant ophthalmologist described the subluxation of the lens, the retinal detachment, and the arrested glaucoma bilaterally. The opinion was that the retinal detachment and glaucoma were caused by the girl's fall down the basement steps. Since the glaucoma was arrested, the vision limited to only the brightest light, and there had lately been no progressive protrusion of the left eyeball, it was not thought expedient to perform an enucleation.

No congenital cardiac anomaly could be detected. A soft, functional, apical murmur disappeared in the erect position; the rate was 108 and was regular. The electrocardiogram was normal with a P-R interval of 0.14 seconds. The cardiothoracic ratio was 10.2/23.3 centimeters. No pulmonary changes were demonstrable by either direct examination or x-ray. The trunk was well developed and a good subcutaneous tissue layer was present. This was

in direct contrast to the emaciated appearance of the extremities. In addition to the appearance of the extremities and hands, as described, there was a "lead pipe rigidity" of the legs and arms, resistance to flexion and extension, and the considerable relaxation of the longitudinal arches of the feet, the latter gave the characteristic pes planus seen in Fig. 2.

The laboratory findings were within the realm of normal: hemoglobin, 80 per cent; red blood cells, 4,360,000 per cubic millimeter; white blood cells, 5,850 per cubic millimeter; blood Wassermann negative; blood calcium, 9.4 mg. per cent; phosphorus, 5.5 mg. per cent; serum cholesterol, 105 mg. per cent. Spinal fluid and urinary findings were normal.

Fig. 3.—D. M., showing osseous appearance in arachnodactyly.

An attempt was made to estimate the level of intelligence with the use of the Revised Stanford-Binet, Form L. All visually determined tests had to be omitted with substitutions, wherever possible, with material which could be appraised by kinaesthetic sensation. She seemed relatively self-assured and was not emotionally upset by separation from her parents. She was cooperative and not apparently depressed by any sense of her inadequacy. Her conversation revealed the paucity of her thought content; there was a noticeable lack of spontaneity; her mood was stable and basically happy. A speech "slushiness" was present. She gave the impression of being dull on a childlike level conditioned by experience derived solely from her limited home environment. A social maturity scale doubtlessly would have revealed a social quotient above the tested Binet mental level. A baseline with his test was determined at the IV-6 year level. Of the 5-year tests given (necessarily omitting the paper folding and man completion) she passed only the sentence recall. Vocabulary and number concept of the 6-year test only could be given but were failed. All 7-year tests except the picture absurdities could be given but were failed. This test, despite its limitations, revealed rather clearly the girl's deficiencies in reasoning, judgment, and memory and depicted the upper level of her ability, when we consider her total lack of any formal didactic training; this provisional scoring of the psychometric test revealed a mental age of approximately 4

years and 11 months and an intelligence quotient of 37. The combination of State Laws pertaining to such mental levels and the ocular defects would necessarily exclude this patient from even the "Special Classes" in our public school systems.

COMMENT

This report traces the progressive development of various anomalies observed in Marfan's syndrome. Although her parents reported her to be normal up to 2 years of age, there are evidences of delayed developmental progress before this age. At 2 years leg braces had to be given to aid in walking. It is problematic whether the fracture of the neck of the left femur was present then or occurred during the following two-year interval when the cast was applied. This fracture appears to have been spontaneous (although the reliability of the parental history could be questioned) and may represent the fragility of the long bones. Failing vision was definitely observed between the fourth and fifth year, but no examining physician deemed it advisable to prescribe glasses. Progressive loss of vision finally shut the girl from the world almost completely. She was not adequately safeguarded. At the age of 12 she fell through an open cellar door and had her visual abnormalities complicated by the head injury which set in motion the retinal detachment and bilateral glaucoma.

We must consider these patients as total personalities whose physical limitations are contributing to their adjustment throughout life. Orthopedic defects should be early remedied so that crippling deformities do not complicate other associated defects. Early recognition of ocular deficiencies should lead to optimum physical correction so that the school placement and adjustment can adequately meet the needs of the child's intellectual capacity and the physical defects.

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THE TREATMENT OF ACUTE SUPPURATIVE PAROTITIS IN INFANTS

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FOR many years the accepted therapy for acute suppurative parotitis in adults has been small doses of x-radiation. This method has been thoroughly successful in curing the condition without the necessity of surgical drainage.

Acute suppurative parotitis in infants has been recently reported by Sanford and Shmigelsky,[1] and the clinical entity adequately described. They found a total of sixty-two cases in the literature including their five cases. They felt that it was probably more common than the literature indicated. Sulfathiazole by mouth and surgical intervention was their treatment of choice.

In the past three years we have had three cases of acute suppurative parotitis in the newborn period, and one case in an older girl which was associated with a generalized staphylococcal septicemia. In all the cases in the newborn period the disease had been contracted one day prior to treatment and all the patients responded promptly in from two to six days. The older child responded similarly but eventually succumbed to the septicemia. Table I briefly summarizes these cases.

TABLE I

	AGE	DURATION SYMPTOMS	TREATMENT	DURATION AFTER R	BACTERIOL.	PAROTID INVOLVEMENT
J. C.	10/12	2 to 3 days	Sulfadiazine Blood: 17.4 mg. per cent Sulfathiazole Blood: 12.3 to 1.8 mg. per cent x-ray 3x	5 days	*Staph. aureus*	Bilateral
T. M.	26 days	1 day	Sulfadiazine Blood: 12.3 to 6.5 mg. per cent x-ray 2x	6 days	*Staph. aureus*	Left
D. E.	9 days	1 day	Sulfadiazine Blood: 3.5 to 1.8 mg. per cent x-ray 2x	5 days	*Staph. aureus*	Left
E. D.	12 days	1 day	Sulfadiazine Blood: 20.8 to 8.1 mg. per cent Penicillin I.M. 10,000 U. stat 5,000 U. q. 3 h. x-ray 2x	2 days	*Staph. aureus*	Right

As can be seen in Table I treatment consisted in x-ray therapy to the involved areas on consecutive days for two to three days. All the cases in the newborn period were treated with sulfadiazine, and one with penicillin also. The

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blood levels obtained with the sulfonamide are noted as also is the dosage of penicillin. The child with the septicemia received first sulfadiazine and later sulfathiazole. This was before penicillin was available. In all four cases *Staphylococcus aureus* was obtained on culture of the pus expressed from the parotid ducts.

In all four patients the parotid involvement disappeared in two to six days without any recurrences. This time period included the period of treatment. This is a much shorter period than that reported by Sanford and Shmigelsky[1] which varied from two to three weeks. Furthermore, this method of therapy avoided surgical intervention and the possibility of a deforming scar or parotid fistula.

Chemotherapy was given these patients as well as the x-ray therapy to control any additional infection that might have been present. In the future, penicillin probably can be used alone with the x-ray therapy especially if *Staph. aureus* is present. In the milder cases without added infection, x-ray therapy alone should be sufficient.

The x-ray therapy of this condition is considered to be a radiologic emergency and should be administered as soon as the diagnosis is established or suspected. It has been our custom to administer 125 roentgens to the involved parotids on the first day. We have used 125 kilovolts, 5 milliamperes, 3 millimeter aluminum filter, and 15 inch target skin distance with a half value layer of 4.6 millimeters of aluminum. A similar dose is given on the second day. If there has been decided improvement, as is usually the case, no further treatment is given. If improvement is slight the roentgen therapy should be repeated on the third day. We have not had to give more than three treatments, but in the rare instances where more radiation is deemed advisable a fourth treatment could be given on the fourth or fifth day. If there has been no improvement by the fourth treatment it is doubtful if any more x-radiation would be of value. In the very unusual instance in which the patient does not respond to roentgen therapy, surgical intervention might be warranted.

SUMMARY

Four cases of acute suppurative parotitis, three of which occurred in the newborn period, are briefly presented and their treatment with chemotherapy and x-radiation is discussed. It is our opinion that roentgen therapy is the treatment of choice in controlling the parotitis and that surgical intervention should be abandoned.

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HEREDITARY SKIN DEFECT IN THE NEWBORN INFANT

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CONGENITAL defects of the skin are rare anomalies found in the newborn infant. Of the cases reported up to now most of them have shown involvement of the scalp. The defects may, however, be found on the trunk or extremities. In these cases they are usually bilateral in location and symmetrical in outline. The condition is present in early fetal life and there is no doubt about its intrauterine origin.

Congenital skin defects have well-defined borders which appear slightly elevated. Microscopic examinations show failure in the development of the epidermis, the skin glands, the smooth muscles, the adipose tissue, and, in rare exceptions, the underlying organs—as the longitudinal blood sinuses. This explains the complete absence of hair in defects which affect the scalp.

The defects are visible at birth. They have been observed in the stillborn child as well as in the normal newborn infant.

The first authentic case of congenital skin defect was reported by Campbell in 1826. Since then not more than 128 cases have been reported. In 1917, Abt published an extensive article on congenital skin defects and gave in table form reports on thirty-eight cases; of these only five involved other parts of the body than the scalp. In 1930, Teruhn discussed the development of amniogenic skin defects in pregnancy and reviewed seventy-six cases in which the head was affected and twenty-nine cases where the body was involved. In 1931, Greig described and discussed in detail the development of congenital defects of the scalp and other parts of the body. Trillat and Cornut, in 1936, and de Vink, in 1938, reported cases where the extremities of newborn infants were affected by congenital skin defects. The most extensive areas involving the trunk were illustrated by Hahn, Adair, and Stewart and by Dowler. Pincherle, in 1938, added a case of his own with congenital cutaneous defect of the scalp that he regarded as ulcerating amniotic disease with lesions still in the state of evolution at the time of birth. In 1942, Anderson and Novy and, in 1943, Quero added two more cases of congenital skin defects. In 1943, Rogatz and Davidson reported a case of congenital defect of the skin and underlying tissues of the scalp and extremities in a newborn infant which proved fatal. They discussed therapy and prognosis of the condition.

CASE REPORT

On July 28, 1942, a girl of Puerto Rican parentage was born at the Flower and Fifth Avenue Hospitals.

The mother had negative serology and had given birth previously to two healthy children. Both the mother and father were 29 years of age. The mother stated on ques-

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tioning that she had a "birthmark" on her scalp. This birthmark on examination was a round area on the occiput about ½ inch in diameter, not retracted, pearly gray in color and shiny and devoid of hair.

The baby was born at term, spontaneously in left occipito-anterior position. Her birth weight was 5 pounds, 14 ounces. The baby appeared perfectly well with the exception of a skin defect over the sagittal suture about two inches above the posterior fontanel. The area of the defect had a raspberry red color and several small nodulated elevations with a shiny surface. There was a complete absence of hair not only over the defect itself but also over a circular area (about ¼ inch in width) surrounding the ulcer. The appearance of the skin around the defect was not normal but whitish and shiny as usually seen in scar tissue. The hair growth around the lesion was definitely centripetal with the ulcer in the center. The complete absence of hair suggested that the defect was not just an injury suffered at birth but rather a congenital skin defect. Ten days after birth the defect had become quite small and the red color in the center had almost gone. The baby

Fig. 1.—Hereditary skin defect.

was discharged on the following day. A recheck on Oct. 16, 1944, twenty-seven months later, showed a well-developed child. The defect on the scalp was completely healed. In its place there was a retracted brownish pigmented area with shiny surface and entirely without hair, about ½ inch in diameter. The area was freely movable over the galea aponeurotica.

DISCUSSION

Congenital skin defects are rather rare. Of the 128 cases reported in the literature most of them involved the scalp. The differential diagnosis from injury is not difficult because injuries are usually not round but irregularly shaped and the hair growth is not disturbed. Syphilitic primary sclerosis acquired intrapartum does not appear until about three weeks after delivery. Pemphigus syphiliticus does not cause a single lesion only. The negative serologic reactions in congenital skin defects excludes syphilis. In epidermolysis

bullosa hereditaria there is a characteristic looseness of the epithelium which can even be removed by slight pressure. The differentiation from an ulcerated encephalo- or meningocele is usually easy, although in some of the cases histologic examination might be necessary.

There are several theories regarding the etiology of congenital skin defects. In very few of the cases was the cause of the defect proved by history and physical findings. A traumatic genesis must be considered rare because of the multiplicity and symmetrical localization of the defects in some of the reported cases. Some authors believe that amniotic adhesions are responsible for the condition. But the fact that in several cases symmetricity of the defects has been reported and that children with congenital skin defects have shown other congenital malformations as syndactylism, speaks against this theory. In addition to that, these synechiae would have to originate from a very early development period (not later than the third fetal week) and in this period a persistent synechia was rarely found. Adhesions between amnion and the fetal scalp in the second half of pregnancy is almost impossible because at that time the development of hair has progressed too far. However, there are reports about a few cases where amniotic bands were found in the immediate vicinity of the defects, sometimes even in direct connection with these lesions. Amniotic bands, therefore, have to be considered as a rare possible etiological factor. Several cases have been observed where congenital skin defects occurred in more than one member of the family. Campbell, for example, in 1826, reported congenital skin defects in two children of the same family and these children had also cleft palates and syndactylism. The case which is reported here is the first one where parent and child showed the same defect over the same anatomical region. This fact strongly speaks for a hereditary character in this particular case.

It can, therefore, be concluded that the genesis of congenital skin defects may be due to exogenous causes (trauma or amniotic adhesions) or due to an endogenous etiology in the cases with a positive family history or with symmetricity of the defects or where other congenital malformations occur simultaneously.

The prognosis of the condition is good where the defect involves only a small part of the body surface or where only the skin and not any other essential organs are involved. Bleeding from the affected longitudinal sinus led, for example, to a fatal outcome in the case of Pincherle. Defect of large parts of the functioning skin as seen by Rogatz and Davidson is fatal. The cause of death in those cases seems to be the same as in other diseases or injuries of the skin extending over a large part of the body surface. The treatment consists of prevention of infection and the application of ointments that stimulate granulation.

SUMMARY

1. A case of hereditary skin defect of the scalp in a newborn girl has been reported. For the first time the same defect in the same location was also found in the parent.

2. Considerations have been given to the etiology and prognosis of the condition.

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GENERALIZED VACCINIA AND PROBABLE INDUCED THIAMINE DEFICIENCY IN A CONGENITALLY HYPOTHYROID CHILD

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THIS paper deals with what we believe is a proved example of generalized vaccinia in a congenitally hypothyroid child and reports the apparent effect of thiamine on some of the toxic manifestations of overdosage with desiccated thyroid.

The patient, a white male 33 months of age, was the fourth of five children. He was born at full term and his delivery was normal. The parents and all of the siblings were in good health and their development was normal. The patient presented definite evidence of hypothyroidism but discussion of this feature of the case is deferred temporarily. He had not received any immunizations and according to his mother's statement he had experienced no recent exposure to any communicable condition. There was no antecedent history of eczema.

On Sept. 29, 1943, the patient became feverish and developed a diffuse erythema involving the inguinal region. The following day clear vesicles formed over the perineum. Twenty-four hours later the external genitalia became markedly edematous and blisters developed on the tongue and lips.

The child was admitted to the contagious unit of Charity Hospital on Oct. 3, 1943. At this time his rectal temperature was 104° F., and it remained high for three days. Subsequently the temperature fluctuated between 100 and 101° F. until the sixteenth day of hospitalization when it returned to normal.

On the day of admission numerous indurated grayish umbilicated lesions, the majority of which were vesicular, were scattered particularly over the external genitalia, the adjacent areas of the thighs, and in the inguinal regions (Fig. 1). In some areas the lesions were discrete and in other areas they were confluent. Otherwise the lesions were remarkably uniform with respect to their shape, size, stage of development, and general appearance. They closely resembled a reaction to vaccinia virus on about the seventh day following a successful smallpox vaccination. All of the cutaneous lesions had an erythematous base and the round discrete eruptions measured approximately 4 mm. in diameter. Similar lesions were present on the tongue, the lips, and the fingers of the right hand. Two days after admission to the hospital vesicles appeared on the hard palate and one was noted on the left cheek. By this time the lesions in the perineum were frankly pustular. Subsequently the cutaneous eruptions developed crusts which later desquamated without leaving scars. Four weeks after the onset of the illness the child's condition had improved sufficiently to justify his transfer to the regular pediatric wards. During this initial period

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Fig. 1.

Fig. 2.

his treatment consisted of the use of bland local applications and the oral administration of 30 grains of sulfadiazine per day.

On Oct. 19, 1943, a biopsy of one of the skin lesions was taken which failed to show Guarnieri or inclusion bodies on microscopic examination. An infectious agent or virus was isolated from the biopsy material. A brief summary of the results of an experimental study of this virus is provided by Table I.

TABLE I. RESULTS OF THE EXPERIMENTAL STUDY OF THE VIRUS RECOVERED FROM BIOPSY MATERIAL

MALE RABBITS	INITIAL AND FINAL WEIGHT (GM.)	DATE OF EXPERIMENT	MATERIAL APPLIED TO SCARIFICATIONS ON EAR*	RESULT	INTERPRETATION
A	2,080	10/21/43	Patient's virus	Excellent take	Material from patient apparently rendered rabbit immune to vaccinia virus
		11/17/43	Vaccinia virus, Batch 1	No take	
	2,180	12/21/43	Vaccinia virus, Batch 2	No take	
B	2,055	10/26/43	Virus from lesion of Rabbit A	Excellent take	Material from lesion produced on Rabbit A by patient's virus apparently rendered Rabbit B immune to vaccine, Batch 1 or 2
		11/17/43	Vaccinia virus, Batch 1	No take	
	2,260	12/21/43	Vaccinia virus, Batch 2	No take	
C	2,035	10/28/43	Vaccinia virus, Batch 1	Excellent take	Batch 1 vaccinia virus viable and apparently rendered Rabbit C immune to virus obtained from lesion on ear of Rabbit A as well as to vaccine of Batch 2
		11/17/43	Virus from lesion of Rabbit A	No take	
	2,120	12/21/43	Vaccinia virus, Batch 2	No take	
D	2,021	10/ 6/43	*Patient's virus (0.2 c.c. intratesticular and 0.2 c.c. subcutaneously)	Subsequent reaction difficult to interpret	Intratesticular and intradermal injection of virus from patient apparently rendered Rabbit D immune to both batches of vaccinia vaccine
		11/17/43	Vaccinia virus, Batch 1	No take	
	2,380	12/21/43	Vaccinia virus, Batch 2	No take	
E	1,110	11/17/43	Virus from lesion on ear of Rabbit A	Excellent take	Material from lesion produced on Rabbit A by patient's virus apparently rendered animal immune to vaccinia vaccine Batch 2
	1,980	12/21/43	Vaccinia virus, Batch 2	No take	
F	1,400	11/17/43	Vaccinia virus, Batch 2	Excellent take	Second batch of vaccinia vaccine viable and produced immunity
	2,060	12/21/43	Vaccinia virus, Batch 2	No take	

*One exception. See data for Rabbit D.

The data in this table show that, first, the material recovered from the patient's lesion produced a definite lesion on the ear of a rabbit (Fig. 2) and that following this reaction the animal was immune to two batches of vaccinia virus each of which was demonstrated by animal experiment to be viable; second, simultaneous intratesticular and subcutaneous injections of 0.2 c.c. each of the patient's virus material rendered another rabbit immune to both batches of smallpox vaccine; third, the material isolated from the scab of a lesion produced on a rabbit's ear by the patient's virus rendered each of two rabbits immune to Batches 1 and 2, respectively, of potent smallpox vaccine; fourth, successful vaccination with smallpox vaccine rendered another animal immune to the virus recovered from the lesion produced on a rabbit's ear by the patient's virus; and fifth, the infectious agent isolated from the patient's lesion could be transferred from one animal to another without altering its immunizing properties. In general these experiments indicated that vaccinia vaccine and the virus recovered from the patient's lesion had identical immunizing properties, and this observation favored the opinion that the child's eruption was a generalized vaccinia. This view was supported by the patient's subsequent failure to obtain a successful take following three smallpox vaccinations using three separate batches of vaccine two of which were shown to be viable through

the typical reactions they consistently produced when used in vaccinating other children in the wards. When it became reasonably conclusive that our patient had a generalized vaccinia re-questioning the mother disclosed the fact his four brothers had been successfully vaccinated against smallpox two weeks prior to the onset of the patient's eruption, and thus the probable source of his generalized infection was established. No attempt was made to demonstrate the presence of protective antibodies against smallpox vaccine in the blood serum of our patient, but without this additional proof we believe his eruption was unquestionably a generalized vaccinia.

Until recently there has been a tendency to classify patients with generalized lesions of unknown etiology and resembling those present in our patient as examples of Kaposi's varicelliform eruption. In some of these cases efforts to determine the etiology of the disease either have failed or have not been undertaken, but in a few instances inclusion bodies indicative of vaccinia,[1] the vaccinia virus,[2] or the virus of herpes simplex[3] have been recovered from varicelliform lesions. These latter observations indicate that a variety of agents or viruses, some of which probably remain to be identified, are capable of producing eruptions which closely resemble one another as well as the so-called varicelliform eruption of Kaposi. An excellent discussion of this general topic and of the pertinent literature is provided in a recent paper by Hershey and Smith.[2]

That our patient presented signs of hypothyroidism has already been mentioned. According to the history he had been chronically constipated since birth. He did not sit erect until after his first birthday and when admitted to the hospital at the age of 33 months he was just beginning ot walk and to say a few words. At this age he weighed 25.5 pounds and his height was 31 inches. As compared with the rest of the body his head appeared to be relatively large. Its occipitofrontal circumference was 48.5 cm. and the anterior fontanel was open. His hair was dry and sparse and his eyebrows and lashes were scanty. The tongue appeared to be relatively large and protruded slightly from the mouth. He had thick lips, sixteen teeth, a sallow complexion, a dry skin, and a generalized myxedema. The abdomen was pendulous, measuring 61 cm. in circumference, but otherwise it was negative on palpation. The patient was very inactive and was mentally sluggish.

The initial blood cholesterol level was 250 mg. and the Wassermann, Kolmer, and Mantoux tests were negative. After the patient had received ¼ grain of thyroid daily for two weeks, additional laboratory studies disclosed the following findings: blood cholesterol, 140 mg.; alkaline phosphatase, 2.1 units; acid phosphatase, 3.2 units; serum calcium, 11.5 mg.; phosphorus, 4.1 mg.; fasting blood sugar, 70 mg. with values of 122, 141, 58, and 64 mg. at one-half-, one-, two-, and two-and-one-half-hour intervals, respectively. In subsequent examinations the blood cholesterol remained consistently below 140 mg. and the alkaline phosphatase reached a maximum value of 8.6 units. An x-ray plate of the wrist and hand revealed a degree of carpal and metacarpal development which in our 33-month-old patient corresponded with the stage of maturation shown in Todd's *Atlas*[4] for a normal male child between 6 and 9 months of age.

The administration of desiccated thyroid was started Oct. 28, 1943, beginning with ¼ grain per day. Subsequently the dose was increased periodically with the result that the patient was receiving 2¼ grains daily by the end of November. The daily dose was then reduced to 2 grains and remained at this level throughout December. During January, 1944, the patient received 2½ grains of thyroid per day and in February the daily dose was increased first to 3 grains and then to 3½ grains. Finally in March the dose was raised to 4 grains per day, but at the end of this month the daily maintenance dose was reduced to 3 grains, and has subsequently remained at this level.

The administration of thiamine chloride and brewer's yeast tablets was started on Nov. 20, 1943, and was continued throughout the major portion of the remaining four months of the patient's period of hospitalization. The quantities given daily ranged from 10 to 30 mg. of thiamine chloride and 1 to 3 yeast tablets.

On this combined vitamin and thyroid therapy the patient's weight declined in the course of four months from 25.5 to 22.5 pounds in spite of his voracious appetite. Experimental studies[5] on rats have shown that an increased food consumption and the administration of thiamine may prevent weight loss in experimental hyperthyroidism, and that injections of pyroxidin (B_6) and calcium pantothenate given during the course of continued thyroid therapy enable animals to regain the weight they lost as the result of hyperthyroidism. The progressive decline in weight exhibited by our patient during a period throughout which he was consuming large quantities of food and was receiving supplements of vitamin B complex as well as desiccated thyroid, resulted chiefly, perhaps, from the gradual disappearance of his myxedema overbalancing whatever effects the B complex vitamins and high food consumption may have had in counteracting the weight loss occasioned by thyroid therapy.

Throughout the first three weeks of thyroid therapy the patient's rectal temperature remained normal, but after November 25, when the daily dose of desiccated thyroid exceeded 1¼ grains he had recurrent attacks of fever of moderate degree. Since these transitory febrile episodes were not accompanied by any detectable evidence of infection they were attributed to the thyroid therapy. Throughout the major portion of the period these mild febrile attacks recurred, the child was taking from 10 to 30 mg. of thiamine chloride and 1 to 3 yeast tablets daily.

From Jan. 21, to Feb. 12, 1944, the administration of thiamine and brewer's yeast tablets was discontinued. During the first seventeen days of this period the daily dose of thyroid was gradually increased from 2¼ grains to 3½ grains and was then held at this level throughout the remainder of February and the first week of March. In this period, during which the child received no vitamin supplement, an episode of fever of several days' duration occurred which was essentially identical to those noted when the B complex vitamins were being taken. It appeared, therefore, that in the doses used, thiamine and brewer's yeast had no appreciable attenuating effect on the mild bouts of recurrent fever which attended the administration of desiccated thyroid.

Two days after the administration of B vitamins was discontinued and when the patient was taking 2¼ grains of desiccated thyroid per day he became sufficiently restless to justify the use of phenobarbital at night for its sedative effect. The restlessness persisted and between February 10 and 13, when the daily dose of thyroid was 3½ grains, the child was extremely irritable. At the time of the onset of the marked irritability a glucose tolerance test was done in association with determination of the pyruvic and lactic acid levels of the blood. The latter study was made by Dr. G. Goldsmith, Associate Professor of Medicine at Tulane University. The glucose tolerance test disclosed the following blood sugar levels expressed in milligrams per cent: fasting, 88; one-half hour, 250; one hour, 184; two hours, 150. These values were distinctly higher than those made when the patient was receiving only ¼ grain of thyroid daily (fasting, 88; one-half hour, 122; one hour, 141; two hours, 58). The pyruvic acid determinations made simultaneously disclosed levels of 1.46, 1.62, 1.57, and 1.45 mg. for the fasting blood and at one-, two-, and three-hour intervals, respectively. The corresponding lactic acid levels were 17.32, 22.67, 14.36, and 17.79 mg.

All of the pyruvic acid levels were higher than the normal fasting level of approximately 1.3 mg. per cent[6] but they did not increase as much as would be expected ordinarily in severe hyperthyroidism.[7] The slight apparent elevation in pyruvic acid and the relatively high glucose tolerance test noted during the period our patient was receiving no Vitamin B complex supplement and was extremely irritable are interpreted as evidence of a slight thiamine deficiency induced, perhaps, by a mild degree of hyperthyroidism.

On Feb. 13, 1944, at which time the patient was taking 3½ grains of desiccated thyroid per day and was very irritable, the administration of thiamine chloride was resumed, giving 30 mg. daily. Thirty-six hours later the patient was in an amiable mood. The daily dose of thiamine chloride and thyroid remained unchanged throughout the remaining half of that month and the first week in March, and during this period the evidence of irritability did not recur.

In general, the observations made on this child suggest that in the dose used the B complex vitamins failed to prevent the recurrent attacks of fever and the progressive weight loss which accompanied thyroid therapy, and that thiamine chloride alleviated the irritability associated with a mild degree of therapeutically induced thiamine deficiency which probably was secondary to overdosage with desiccated thyroid.

Eighteen days after the administration of thiamine was resumed, the patient was exposed to measles, and developed the disease on March 16, 1944, in spite of a prophylactic injection of immune placental globulin. He left the hospital twelve days later on a maintenance dose of 3 grains of desiccated thyroid per day and has continued on this therapy. During the period of nineteeen months the patient has been taking desiccated thyroid, his height increased from 31 to 36¼ inches and his weight increased from 25½ to 34 pounds. At the age of 52 months his intelligence quotient was found to be 60 by Professor Paul C. Young, Director of the Department of Psychology at Louisiana State University.

SUMMARY

An example of generalized vaccinia in a congenitally hypothyroid child is reported.

A virus was isolated from one of the patient's lesions. Animal experiment revealed the immunizing properties of this virus to be identical to those of vaccinia virus.

The administration of thiamine chloride promptly relieved marked irritability attributed to thiamine deficiency induced by overdosage with desiccated thyroid.

The administration of B complex vitamins had no appreciable effect on recurrent attacks of mild fever which accompanied thyroid therapy. These supplementary vitamins and a voracious appetite also failed to prevent weight loss during the first four months of thyroid therapy.

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THE GREENBERG MODIFICATION OF THE FLAGG LARYNGOSCOPE—ITS USE IN ASPHYXIA NEONATORUM

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MANAGEMENT of asphyxia of the newborn infant frequently necessitates direct visualization of the larynx for both diagnostic and therapeutic purposes.

Laryngoscopy of the newborn infant has always presented a particularly difficult problem owing to (1) need of special skill (2) absolute prerequisite indication for its use and (3) fear of increasing trauma and consequent dangers especially present in the premature and newborn infant. These difficulties have been the cause of laryngoscopy and its related procedures being relegated to the otolaryngologist or anesthetist especially trained in its use. Experience has shown that the time element required in obtaining such consultation has been a deciding factor in the life of the patient already handicapped by failure of development, trauma of delivery and pathologic physiology associated with these and other causes of asphyxia. The laryngoscope made in 1938 by the Welch Allyn Company, Auburn, N. Y., as the Greenberg Modification of the Flagg Laryngoscope has been made for this purpose.

The following is a summary of the advantages of the new type of laryngoscope with description of its use:

1. Easier approach to the larynx—the speculum is passed in midline and slid down the tongue to the epiglottis.

2. Immobilization of the tongue without effort—the tongue comes to rest in the longitudinal trough of the lingual surface of the speculum which is concave rather than convex.

3. Relatively atraumatic immobilization and elevation of the epiglottis exposing the rima without undue tension and consequent distortion of the rima—the epiglottis is lifted up out of the field of vision by the tip of the concave lingual surface on the terminal end of which the tubercle of the epiglottis comes to rest. The relative ease of this procedure diminishes the likelihood of increasing edema as a result of the procedure itself. It also decreases the danger of cardiac complications resulting from vagus stimulation when forceful traction upward and forward is exerted on the epiglottis.

4. The ease of the passage of this instrument and ready localization of structures make repeated passage of the speculum unnecessary.

5. The field of vision is increased because of the retraction of the adjacent tissues by the slight upward tilt of the lateral angles of the speculum.

6. Retaining the features of the Flagg Laryngoscope which permits the pasage of instruments for intervention from the right side as well as in midline.

This instrument will not be available again until after the end of the war owing to the lack of available facilities for its production at present.

Fig. 1.

Fig. 2.

7. The common difficulty of the tongue falling into the lumen of the laryngoscope and obstruction of the view is avoided by the immobilization of the tongue.

The following cases are selected to show ordinary types of asphyxia neonatorum and use of the modified laryngoscope.

Baby J. T., normal male child, on the eighth day of life, during the course of the 2 P.M. breast feeding, belched, vomited, was unable to inspire any air, developed cyanosis, convulsions, and finally went limp. The nurse on the floor responded to the mother's call and carried the baby to the treatment room of the nursery where laryngoscopy and intratracheal aspiration had just been completed on another newborn infant, Baby D. D., whose case will follow. Baby J. T. was immediately placed in position for laryngoscopy, i.e., pad under shoulders and neck extended with vertex on table. (I have not found the head flexed on chest with chin depressed position satisfactory in infants.) Owing to the extreme character of this emergency, the instruments used could not be sterilized from one patient to another. The laryngeal speculum was slid down the tongue to the epiglottis. The epiglottis was then elevated revealing a clot of curdled milk completely obstructing the rima glottis. Considerable milk was noted in the hypopharynx and it was suctioned away. Straight metal suction tip was used to grasp the clot obstructing the rima glottis and by gentle traction the clot was removed. Milk was then noted in the trachea and was also suctioned away. Artificial respiration was instituted by rhythmic thoracic pressure and the baby responded momentarily with a few spontaneous gasps. Baby J. T. then developed generalized twitching, then breathed spontaneously but with difficulty which progressed with deepening retractions of thoracic structures and convulsions recurred. Laryngoscopy was then repeated and a large clot of milk was noted below the rima glottis. This was removed in a like manner and intratracheal artificial respiration was instituted by attaching the Flagg machine to the intratracheal tube, working the vent to operate rhythmic positive intrapulmonic pressure. The baby then responded and this time breathed quite easily. No stimulating injections were given. Baby J. T. was put in Trendelenburg position with oxygen for twenty-four hours. Full nursery routine was then followed with the baby off breast and he was discharged on the eleventh day as a normal newborn infant.

Baby D. D. was delivered by internal podalic version in the management of transverse position with prolapse of the left arm. She attempted spontaneous respiration with extreme retraction of the sternum and interspaces. Emergency aspiration of meconium and amniotic fluid from the pharynx was done by the obstetrician and the newborn infant was placed in an incubator and given continuous oxygen. Two hours after delivery, she was examined. Skin was pallid, lips of good color, heart rate 166 per minute; respiration very shallow, rapid, wavering in character with occasional gasp, and "cephalic" cry was noted. Auscultation of the chest revealed breath sounds throughout the entire left chest and right upper chest and an absence of breath sounds in the right chest from the third interspace down, in which area only transmitted heart sounds were heard. All extremities were spastic with "lead pipe" type of spasticity greater on the left side than on the right. Nuchal resistance was present but no rigidity was noted. Tonic neck reflex was not elicited owing to the nuchal resistance. Removal of the newborn infant from oxygen for three minutes caused an increase of spasticity, no change in respiration, increase of heart rate to 250 per minute and cyanosis of the lips. Oxygen was readministered for twenty minutes. Laryngoscopy was then done which revealed normal laryngeal structures, rima glottis patent, meconium stained fluid and blood present in the oral pharynx and, when removed, similar fluid was noted to come from the larynx. A straight metal tube was inserted intratracheally and gentle suction was applied as far down as the carina and maintained momentarily. One dram of meconium stained fluid was so obtained. The baby was replaced in the incubator with oxygen, in Trendelenburg position. The diagnosis of atelectasis of the right lower lobe and intracranial hemorrhage causing transmission of increased pressure about the respiratory center was made. Baby D. D.

has progressed favorably. The spasticity of the left upper extremity has gradually disappeared over a period of three months but tends to recur with fevers associated with ordinary illnesses. Baby D. D.'s mental development is normal.

Baby F. C., white, male newborn infant, normal left occipito-anterior forceps delivery, was seen on the third day of life with history of recurrent asphyxial attacks precipitated by attempts at feeding, changing of position, skin stimulation, or other stimuli. Generally, the baby was well developed in appearance; skin was clear; cord, attached and dry; no tremors or convulsions were noted except during the attack; respiration was regular, rapid, very shallow; color good; heart rate 120 to 126 per minute rapidly increasing to 140 to 144 per minute when disturbed for examination. The baby moved all extremities spontaneously. Some conjunctival hemorrhage was noted. When the baby was disturbed as with examination, a weak, muffled "cry" could be barely heard. Further disturbing of the child, as with slapping the soles of the feet, resulted in an attempt at more vigorous respiration, with resultant sternal, intercostal, costal, and subcostal and suprasternal retractions, and breath sounds changed from shallow, regular breathing with phases of respiration continuous with each other to very short inspiratory phase followed with a period of pause, then followed by a barely elicitable expiratory phase. As the attack continued with further struggling for air, cyanosis and convulsions developed. The diagnosis was made of obstructed respiration with conversion from partial to complete obstruction as with partial stenosis of the larynx. This was considered indication for intervention. Laryngoscopy revealed rima glottis distorted with attempted inspiration causing inversion of the ventricular folds. The only laryngeal structures not sucked into the trachea were the corniculate prominences which appeared approximated. When final attempt at expiration occurred, the position of the corniculates did not change. No arytenoid notch could be noted and the ventricular folds were noted to be adherent to each other except for a minute opening approximately one-eighth inch in length situated at about the center of the line of fusion of the ventricular folds. The tip of a straight metal suction tube was placed against this opening and was gently forced through so establishing a more patent airway with resultant almost immediate relief of difficult respiration. The adherent ventricular folds were then freed by exerting gentle pressure upward and downward until the structures assumed a more natural appearance. The greatest amount of pressure in this simple method of blunt dissection was used to effect a separation of the corniculate prominences which when done resulted in the formation of the interarytenoid notch. Milk was found within the trachea and was removed. The possibility of co-existent tracheo-esophageal fistula was excluded at a later time by x-rays and fluoroscopy with radiopaque feeding. Progress was uneventful and the child acted normally except for a hoarseness, which persisted for approximately ten days.

This article presents the Greenberg Modification of the Flagg Laryngoscope to further facilitate its use in cases of asphyxia neonatorum as caused by laryngo-tracheal obstruction with foreign material, congenital stenosis of the larynx, atelectasis and concomitant intracranial hemorrhage.

The Social Aspects of Medicine

COMMUNICATIONS ON THE PEPPER BILL S.1318
A MEDICAL CARE CREDO—MEDICAL EDUCATION

Boston, Mass.,
November 8, 1945

Dear Dr. Park:

On July 26, 1945, Senator Pepper of Florida introduced into the Senate a bill (S.1318) "To provide for the general welfare by enabling the several States to make more adequate provision for the health and welfare of mothers and children and for services to crippled children and for other purposes." The bill was referred to the Committee on Education and Labor and hearings will be held in the near future. This bill should be read carefully by all pediatricians as it will influence materially their future activities. Copies may be obtained by writing to one's State senator. At the time of introducing the bill, Senator Pepper made a speech analysing the bill and commenting upon its provisions. This speech is also worthy of reading and study. Copies may be obtained from the United States Government Printing Office or one's senator. The Bureau of Legal Medicine and Legislation of the American Medical Association has prepared an analysis of the bill which was published in the Journal of the American Medical Association, on August 11, 1945. In discussing the Pepper Bill, as it is commonly designated (the official citation is the "Maternal and Child Welfare Act of 1945"), I shall quote freely from Senator Pepper's speech.

The bill contains five titles—I. Maternal and Child Health Services. II. Services for Crippled Children. III. Child Welfare Services. IV. Administration. V. General Provisions.

Senator Pepper says in his introductory statement: "The war has given us irrefutable proof that a nation which neglects the health and welfare of its children does so at its own peril" and "indifference to what happens to children sooner or later strikes at the very life of the nation." And again, "The Nation's greatness in peace is measured by the opportunities open to its citizens for health, personal satisfactions, and the exercise of social responsibility. These opportunities can be assured only if children have their full chance for physical, mental and emotional growth and well-being." "But the individual family alone cannot buy health for its children. Community as well as family resources are needed. * * * * Step by step, over a period of the next ten years, the bill makes possible the enlargement and strengthening of these public services in accordance with the requirements of each State." At this point Senator Pepper raises the issue—opens the door for diverging points of view. Most of us would wish that each family in the Nation might be entirely self-sufficient—able to provide for its needs. Such an economic structure would be ideal—but facts indicate clearly that large portions of the population cannot, from their own resources, secure the benefits which are available to those in a more favored financial status. If one subscribes to the thesis that all children have the right to the opportunity for optimal conditions for growth and development (and pediatricians have been proclaiming this thesis for many years) the problem resolves itself into how these opportunities are to be provided. If the family cannot provide them, then the community must assume the obligation. The community can do this either by voluntary effort, or by governmental action. Voluntary effort has done much to stimulate interest in the welfare of children and has initiated many activities in their behalf. One would wish to see such efforts continue and expand, but when one considers the magnitude of the undertaking if all children are to be reached, it is inconceivable that voluntary effort alone can accomplish the task. Government must assume a share of the burden. Our concern should be that this share is wisely administered and that the desired goals are effectively attained.

The Pepper bill "makes Federal financial aid and technical assistance available to the States for the purpose of providing medical care and health services for mothers and children and child-welfare services for emotionally sick and insecure children and for children without parental care or supervision. It stipulates that these services shall be *available to all who elect* to participate in them, regardless of race, creed, color, place of residence, or national origin."

There is raised by the last statement the recurring question of "ability to pay," the so-called "means test." It is a knotty problem. There is no means test in the educational opportunity offered to children. Those favoring this legislation ask why should there be any limitation in relation to health opportunities? The persons rendering the educational services —teachers—are paid on a salary basis. Their salaries are in general small in relation to the importance of the work and the auxiliary facilities are often inadequate or nonexistent. The quality of service has suffered in part at least from these considerations. Health services have been rendered in the past in large measure on an individual basis by physicians who have received compensations of varying amounts but in nearly all instances at a higher level than teachers' salaries. Auxiliary health facilities have been provided to a greater extent in relation to medical care than in connection with education except in association with privately endowed institutions. The quality of medical service has benefited thereby. Governmental health services have expanded greatly in recent years. The quality of those services has been good for the most part and excellent in many divisions. Auxiliary facilities have been adequate but compensation for personnel has been small except in the higher positions. Unless some provision for a means test is introduced as the government expands its medical care program, those rendering the service will inevitably suffer a reduction of income. This may be less than anticipated, for many persons now receiving free care will become "pay patients" through governmental support. But such patients will require as much time for care as those now paying from their own resources at a higher rate.

The bill stipulates that in order to provide "for a high quality of (medical) care" there shall be "adequate remuneration for the persons and institutions providing medical care and related services; opportunities for postgraduate training of professional and technical personnel; and such use of health centers, hospitals, clinics, and health service agencies, public and voluntary, as will achieve the satisfactory distribution and coordination of preventive, diagnostic, consultative, and curative services for mothers and children furnished by general practitioners, specialists, public health personnel, laboratories, and others."

If physicians receive a substantially smaller income, will the quality of the service suffer? I believe that it will unless the differential is small and the additional security and the availability of auxiliary services are enough to offset it. Many of the medical services other than physicians, especially hospitals, would benefit by the bill, for "free patients" would disappear. The availability of facilities should raise the quality of medical care.

The application of a means test involves many complicated administrative problems which require and will receive careful study. It is to be hoped that some satisfactory solution may be found whereby those able to pay either on a fee-for-service basis or through prepaid voluntary insurance may do so. The government would then assume financial obligation only for those below this income level, or to supplement family resources when necessary.

The bill provides specific amounts of money for the first fiscal year but thereafter for the following years amounts to be appropriated as may be required to carry out the purposes of the act. This allows great expansion or retrenchment of the program but seems a wiser provision than to set the amounts at this time when the needs could be only inaccurate guesses. It is recognized that very large appropriations will be required to carry out the program.

The money is to be expended through grants in aid to States who must match the Federal grant dollar for dollar from State or State and local funds and will be administered through the State health agency. It is to be used "primarily to pay doctors, dentists, nurses

and other professional personnel for services and care to mothers and children. It will pay for care in physicians' offices, hospitals, convalescent homes, clinics, or in the home.'' In developing the State plan under this bill it is stipulated that it shall be coordinated ''with the general public health and medical care program of the State health agency.''

The act is to be administered by the Chief of the Children's Bureau with an Advisory Committee. This form of administration is a natural provision under the present governmental setup. The bill is, in fact, an extension of many services already carried on by the Children's Bureau but adds others not now rendered. The question of the reorganization of the health services of the Federal Government with consolidation into a single Department of Health is involved in the consideration of this bill. It seems to me, however, that it is not a determining factor in one's attitude toward the bill and need not be discussed at this time.

Title I is the portion of the bill most directly affecting pediatric practice and most likely to involve the widest differences of opinion. Its provisions have been covered briefly in the foregoing discussion. What attitude should one take in relation to it? I can only state my own position. Every physician and especially every pediatrician should study the bill himself and reach his own conclusions. After as careful thought as I have been able to give to the matter and after discussions with many other physicians, I have come to this conclusion. I am in complete sympathy with the objectives of the bill. I believe it is an honest attempt on the part of its sponsors to improve the care of children. The bill as at present written must have several modifications to make it acceptable legislation.

First. I would like to see a clarification of language in Section 101 so that the various States might develop the program gradually undertaking only those services which could be performed adequately. At the same time some time limit would probably have to be included to prevent a laissez-faire attitude by any State and also some provision as at present, whereby, if a State did nothing, the Federal Government might initiate the program.

Second. I should like to have definite assurance that the program may vary widely in different States. There should be no over-all Federal pattern which must be followed by a State to have its plan approved. Liberal adapation of an ideal plan to local situations should be clearly recognized as allowable. This should include the setting of fee schedules by the State agency taking into account local conditions, but perhaps subject to review by the Federal agency.

Third. I should like to see some formula introduced whereby ''ability to pay'' would be recognized and governmental participation limited to those situations in which the family was unable to provide the medical care.

Fourth. The Advisory Committees at both the Federal and State levels should be given the opportunity to make public their recommendations even though such recommendations might not be adopted by the Administrative Officer. The Advisory Committees with professional representation should be active participants in the development and operation of the program, and the medical profession should have some voice in the selection of its members.

Title II dealing with Crippled Children seems to me satisfactory if similar modifications are provided as advocated for Title I.

Title III is not directly a medical program and may be passed by without comment at this time.

Titles IV and V deal purely with administrative procedures.

Richard M. Smith, M.D.

Des Moines, Iowa
November 9, 1945

Dear Dr. Park:

Thank you for your wire of November 6 inviting me to express my views on the Pepper bill for publication in your column in the forthcoming issue of the JOURNAL OF PEDIATRICS. You will appreciate, I am sure, those considerations—shortness of time, limitation of space—which make it desirable for me to limit my remarks largely to matters of mutual interest to the Academy and the Children's Bureau.

There are a number of reasons why I am opposed to the Pepper bill. Chief among them is my regret that it again raises an issue between many of the practicing pediatricians of the country and the Children's Bureau. Up to the time of the publication (by the Children's Bureau) of the report of the National Commission on Children in Wartime, followed shortly by the recommendation of this report practically in toto to the President by the Secretary of Labor as one of her last acts in office, and this in turn followed by the introduction of S.1318 into Congress by Senator Pepper and his colleagues, I had been going along under the impression, as I am sure had the majority of the members of the American Academy of Pediatrics, that the EMIC program would end six months after the close of the war and that the development of a postwar child health program would be a cooperative effort based upon the comprehensive survey recommended in the report of the "Committee of Nine" and unanimously accepted by the Academy of Pediatrics at its St. Louis meeting a year ago. The objectives as stated in that report of making "available to all mothers and children in the U. S. A. all essential preventive, diagnostic, and curative services of high quality . . ." are similar to those expressed in the Pepper bill and, so far as I am aware, have the full approval of all medical persons. But opinions as to the methods by which they should be pursued differ. As you know, the survey is now in active progress under the able chairmanship of Dr. Warren Sisson. At its conclusion much should be known as to the actual need for extension of facilities, personnel (physicians, nurses, health officers, technicians), and for dissemination of information to acquaint people in the better use of available facilities and in a better knowledge of what good medical service consists. A postwar national child health program based upon need as demonstrated by this survey would, I believe, have the full support of the practicing pediatricians of the country. The interjection of the Pepper bill has had the effect of dampening the enthusiasm of many of us, however, and we find it difficult to escape the conclusion that S.1318 is merely another planned step in the independent program of the Children's Bureau. Lest there be any misunderstanding, let me state here that I believe the Academy's survey will be of great value as a guide to obtaining the objectives previously alluded to, but I should like it much better if the allocations under the Pepper bill were to wait until they could be fitted into demonstrated needs rather than to be used to continue the EMIC program, the administrative rulings of which were so objectionable to so many physicians.

The proponents of the Pepper bill appear to be making much of the statement that if education is a responsibility of government then so is the health of the nation. To my way of thinking this is simply another way of saying they favor a national system of medicine under governmental control; in other words, state medicine. In fact, many of us who are engaged in the private practice of medicine are of the belief that if the Pepper bill is passed by Congress, and if the Children's Bureau continues administrative regulations similar to those in effect under the EMIC program, the die will have been cast in the direction of state medicine from which there will be no turning back. It will be a question of time only until the medical care of the entire nation is controlled and financed by the Federal Government. I am of the opinion that as yet the nation as a whole is not ready to accept that this is the type of a national health program it wants.

While the administrative regulations to be formulated by the Children's Bureau for the dispensation of funds allotted under S.1318 have not as yet been made known (and may I interject here that I believe they should be before hearings are held on the bill and

before it is voted upon in Congress), nevertheless it is difficult to see how $50,000,000 could be spent for maternal and child health services unless a procedure similar to that employed under the EMIC program is followed. Obviously this amount of money spread among the 40,000,000 children in the nation under twenty-one years of age, plus that portion which would go for maternal care, would not in the first fiscal year greatly influence the pediatricians' private practice, but the provisions of the Pepper bill are such that little room is left for doubt but that once started appropriations would be constantly raised until all fees, or a major portion thereof, for pediatric practice would come from governmental funds. That this is desirable either from the standpoint of standards of pediatric practice or individual initiative and independence is certainly open to serious question. At any rate it is my conviction that a majority of the pediatricians of the country do not look with equanimity upon the prospect of a single governmental bureau in Washington playing such a major role in their practices as to include among other things the setting of arbitrary fees which they may receive for their services. Cooperation of physicians under the EMIC program was forthcoming because of the patriotic factor involved. With this factor removed, as it will be in the postwar period, it is my feeling that a somewhat less cooperative attitude may be encountered.

Then, too, I cannot find myself in sympathy with the administrative policy of the Children's Bureau of dispensing governmental funds without regard to economic need. Even a means test of sorts was used in the EMIC program, since only enlisted men in the first four grades qualified for federal benefits, but under the Pepper bill any pregnant woman or any child under twenty-one years of age, regardless of economic status, is eligible to receive free medical service at governmental expense. This is wasteful of federal funds and therefore uneconomic. In my judgment governmental funds should be used in those localities and where there is demonstrated need.

To be considered, too, under the Pepper bill is the effect free maternal care and free medical care for all children may have upon the teaching medical centers of the nation from the point of view of availability of teaching material. It is well known that in good times attendance at free clinics and in free hospital wards falls off. People prefer the services of private physicians when they can afford them. It would be a serious situation indeed if one of the effects of the Pepper bill should be to so reduce teaching material as to interfere with the best training of obstetricians and pediatricians.

Statements to the effect that we can no longer afford to neglect our mothers and children, or that there are so many thousands suffering from crippling diseases who are not receiving medical care, or that lives are being lost because mortality rates in one state are higher than they are in others are likely to be misleading, particularly when used to create the impression that a measure like the Pepper bill would very shortly correct the situation. Maternal and infant mortality rates have fallen rapidly in the last quarter of a century until today the American people enjoy the highest standard of medical care of any nation in the world, but no one I think would contend that these low rates are the result of the EMIC program. In recent years the general medical profession, with the pediatricians in the vanguard, has attacked with vigor the problem of increasing and extending medical facilities and medical services to attain the objectives desired by all of us—all essential preventive, diagnostic, and curative services of high quality for everyone in the United States. One needs to mention only such voluntary insurance programs as the Blue Cross, state medical service programs, and insurance programs of individual industries. The Hill-Burton hospital bill, if enacted into law, will provide health center and hospital facilities which, together with our well-trained physicians leaving our medical schools and hospitals of today, will go a long way toward solving the problem of bringing good medical service to rural areas. Most states within their own borders have developed medical service programs at state and local levels which are effectively lowering mortality rates and raising health standards. One might venture that states like Connecticut and Maryland in all probability owe their enviable mortality records largely to the influence exerted by two of the top-ranking medical schools of the country situated within their borders plus excellently worked out state pro-

grams for the health of their people. They offer splendid examples for the emulation of states with higher mortality rates, but the opinion might be advanced that more will be required to achieve like results than providing free maternal care and free medical service to children.

In this effort to improve and extend facilities and standards of medical care for the American people, it should be the function of governmental agencies to assist and support private enterprise rather than to initiate programs which antagonize and which threaten to supplant what people are trying to do for themselves.

May I conclude this by saying that I am opposed to the Pepper bill, or to those portions of it which would grant the Children's Bureau sufficient funds to pay doctors for the care of mothers and children (including crippled) who are financially able to care for themselves because (1) I believe it would be a sounder policy to build a postwar child health program in cooperation with the pediatricians of the country on the basis of need as demonstrated at the completion of the Academy's survey; (2) I believe its provisions are such that its passage by Congress would inevitably lead to state medicine; (3) I believe that once started the appropriations would increase year by year until shortly the private practice of pediatricians so far as its financial aspects are concerned would be entirely a government function; (4) I cannot agree with the Children's Bureau's administrative policy of dispensing government funds without regard to economic status; (5) there would appear to be a risk in free maternal care and free medical care to children that training of obstetric specialists and pediatricians might be interfered with; and (6) efforts are under way, initiated by private enterprise, which hold every promise of achieving desired objectives on a sounder and more democratic basis, providing they can be allowed to develop without interference by programs initiated by the government.

Cordially yours,

Lee Forrest Hill, M.D.

COMMUNICATION

Boston, Mass.
November 5, 1945

Dear Dr. Park:

Dr. Joseph Wall's letter to you which was published in the October issue of the JOURNAL OF PEDIATRICS deserves comment because it contains statements which, though frequently made by physicians, are susceptible of interpretations that might subject the profession to the criticism of being unduly narrow in its point of view. As Dr. Wall uses the English language in a manner that arouses envy in most of us, and particularly in myself, you may well wonder at my temerity in questioning the clarity of his written words. The possible justification may best be indicated by reference to specific statements.

In the first two paragraphs, what is meant in stating that the advances in the science of pediatrics together with the widespread cooperation of pediatricians have been largely, if not solely, responsible for the attainment of better child care in the United States? Does this mean that the pediatrician has accomplished by idealism and self-sacrifice far more than should have been expected of him or merely that pediatricians have participated in advances in a field which was their responsibility? Does it also mean that the City, State, and Federal public health and welfare agencies have fallen down on their jobs?

Just what is meant by the statement that "there has been during recent years an alarming encroachment upon the rights and prerogatives of physicians on the part of governmental agencies under the guise of social betterment"? What rights and prerogatives have been encroached upon? The right to do what physicians want as regards the health of people or as regards the purely personal affairs of physicians? And has the specified encroachment been deceitfully accomplished under the guise of social betterment or wisely accomplished as a necessary step in improving medical care? Have governmental agencies encroached upon the rights of physicians to a greater extent than the voluntary agencies or voluntary non-

profit and so-called "commercial insurance" schemes? Is this encroachment affecting the individual liberty of physicians more than the social changes of today inevitably are affecting the liberty of others? Have or have not the people through their freely and democratically elected representatives the right to enact legislation which they believe enables them to reduce the hazards and financial burdens of illness? How much independence can doctors demand ethically, legalistically, or financially in the practice of a profession whose very existence depends upon the misfortunes of others?

Can it be stated with certainty that the Pepper bill threatens the existence of pediatrics? May it not be the means of financing pediatrics far better than we have been able to in the past?

Did Senator Pepper in his press release of July 26 mean to imply that the Academy had endorsed his bill in detail or merely endorsed its objective, which in Senator Pepper's opinion coincides with the objective for child health in the postwar period unanimously adopted by the American Academy of Pediatrics at its annual meeting in St. Louis, 1944?

Would the Pepper bill really "confiscate the intellectual abilities of physicians"? Or might it be the means of financing facilities which would permit the physicians a better opportunity to use their intellectual abilities?

Do the statements concerning a "means test" reflect a sound consideration of this important subject? Because the income tax is based on income does it follow that a "means test" must be applied to activities financed by tax funds? Must we apply a "means test" to our public schools?

Is it correct to refer to the indiscriminate extension of "*free* medical services"? Is it not probable that fewer people will receive *free* medical care under the provisions of such a bill as Senator Pepper suggests than receive free care today? Is it not almost certain that physicians would be paid for rendering care which they render without remuneration at present? Are we sure that it is wise to object vigorously to an extension of orderly financed medical services?

Why should we insist that the burden of charity medicine be left to the physician? Does "Federal, State and Municipal participation in" child clinics and health conferences threaten "to engulf" us or to relieve us of a charity burden that has become excessive? Is it the Pepper bill or the insistence of physicians upon a continuation of individualistic fee-for-service practice under the changing circumstances of society today that, as Dr. Wall says, "unwittingly builds a Frankenstein which now threatens to rise up and destroy us and the specialty of pediatrics to which we are devoted"?

Until thoughtful consideration and tolerant debate have provided us with answers to these and other questions, can we as individuals afford or can the Academy with wisdom adopt an uncompromising attitude toward such a bill as S. 1318? How unfortunate if hasty and intolerant action on this important matter deprives pediatricians of an exceptional opportunity to continue their leadership of the profession in the provision of better medical care.

Respectfully,
Allan M. Butler, M.D.

Asbury Park, N. J.
October 31, 1945.

Dear Dr. Park:

Having realized for many years the importance of having our American Academy of Pediatrics promote the cooperation of governmental and medical agencies for better child health, I am enclosing "10 Beliefs of Our Medical Profession," which I trust you may print in your Column in the JOURNAL OF PEDIATRICS for the consideration of the Fellows prior to our annual meeting in Detroit in January, 1946, which meeting will be largely devoted to the "social aspects of pediatric medicine" as embodied in the Pepper and Wagner-Murray-Dingell bills.

I am sure that you will agree with me that cooperation on the part of governmental and medical agencies on behalf of better child health involves a thorough and democratic airing of the pros and cons of the subject matter on the part of all concerned with child health, and you will note that the objective of this presentation is the creation of a continuing conference, where differences of opinion as to methods may be solved. I have spent the last three months in the preparation of this "Credo" and feel that I have in some measure succeeded in crystallizing what most doctors are thinking today. . . .

Sincerely yours,
Stanley Nichols, M.D.
Chairman, Committee on Cooperation with Governmental and Medical Agencies, American Academy of Pediatrics.

A MEDICAL CARE CREDO OF THE MEDICAL PROFESSION—TEN BELIEFS OF ORGANIZED MEDICINE AS TO MEDICAL CARE

MEDICAL RESPONSIBILITIES

1. WE BELIEVE, that, in the same manner that a physician is doctor of his individual patients, and feels a definite responsibility for their good health and medical care; every county medical society, collectively and figuratively speaking, is the doctor of the people of its county; every state medical society is the doctor of the people of the state; and the A. M. A. is the doctor of the people of the nation—and all feel a definite responsibility for the health and quality, quantity, availability, and distribution of medical care for the American people.

SOLUTION OF THE MEDICAL CARE PROBLEM

2. WE BELIEVE, that, in order to see that good quality medical care is provided for the American people, as well as a continued improvement in the quantity, availability, and distribution thereof, it is essential that a real teamwork medical care conference in the public interest, organized on a complete basis of equality, good faith, and good will, is promptly created by the medical profession or the government (or preferably by joint action), instead of the present murky atmosphere of mutual suspicion and distrust which now exists.

THE PARTICIPATION OF ORGANIZED MEDICINE

3. WE BELIEVE, that the quality of medical care in any governmental administered health service program involving the public and the medical profession is now and will be in direct proportion to the voluntary participation of the medical profession in both the formulation and administration of such programs.

THE PUBLIC AND MEDICAL CARE

4. WE BELIEVE, that the American people want good quality medical care. They also want it made more available to everyone.

THE MEDICAL PROFESSSION AND MEDICAL CARE

5. WE BELIEVE, that the medical profession is insistent on rendering good quality medical care. They also are working to make it more available to everyone.

THE SOCIAL ENGINEERS AND MEDICAL CARE

6. WE BELIEVE, that the nonmedical and medical social engineers who proposed governmental medical care and (1) the social agencies, (2) labor organizations, and (3) governmental agencies who have espoused and promoted governmental medical care to be paid for by the compulsory taxation of every citizen of the United States, are chiefly and primarily concerned with quantity, availability, and distribution of medical care. They are also secondarily interested in the quality of medical care.

FACTORS IN MEDICAL CARE QUALITY

7. WE BELIEVE, that, except in the patriotic rendering of medical services in time of war and a few other scattered instances, there are certain definite factors which usually produce definite deterioration in the quality of medical care under government auspices. These definite and inescapable factors are:

(1) The great difficulty of securing able (Class A) physician personnel,
(2) Too many patients per hour,
(3) Unsatisfactory physician-patient relationship—(Lack of that time-consuming and all important psychological and psychiatric factor which allows physicians to relieve mental tensions and anxiety in their patients),
(4) Low rates of compensation,
(5) Multiplicity of governmental rules, regulations, and reports (so-called governmental red tape), which hamper the rendering of good medical service.

We believe these are the five factors that caused the recent difficulties as to the quality of medical care rendered veterans by the Veterans Administration facilities as testified to by government officials. We believe that these are the five factors which do and will make any program of governmental medical care result in mediocre quality unless the organized medical profession is immediately given a permanent and equal share in the formulation, revision, and administration of all governmental medical programs, which affect the general public. We believe that such an equality of cooperative effort on behalf of the best possible quality, quantity, availability and distribution of medical care for our American people by medical and governmental agencies, is in correct and full accord with the principles of American democracy and should be instituted forthwith.

THE WAGNER-MURRAY-DINGELL AND PEPPER BILLS AND THEIR EFFECT—NONPARTICIPATION OF MOST GOOD PHYSICIANS

8. WE BELIEVE, that, because the medical profession (organized medicine) has not officially participated in the formulation of the Wagner-Murray-Dingell and the Pepper bills, and, because these bills give the medical profession no share in the administration thereof, the majority of most able physicians will not participate in these proposed programs of governmental medical care because the average quality of medical care would be mediocre or low grade.

THE WAGNER-MURRAY-DINGELL AND PEPPER BILLS' UNHAPPY EFFECT ON PHYSICIANS' TYPES OF PRACTICE—THE WISE CHOICE OF THE PUBLIC

9. WE BELIEVE, that the passage of these or similar bills, by the efforts of social work or labor groups in this country, which do not provide for the participation of the organized medical profession in the formulation and administration thereof, would inevitably and unfortunately for the public result in the creation of two kinds of physicians in this country—private doctors and government doctors. We believe the great majority of able physicians will stick to private medical care because they have in the past, and will in the future insist on conditions which permit the rendering of good quality medical service to the public. In this connection, we believe that the American public today largely know the difference between good quality medical service and mediocre quality medical care as evidenced by the marked wartime increased demand for individual private medical service and greatly decreased attendance at most types of clinics.

THE MEDICAL PROFESSION'S PRESCRIPTION FOR IMPROVEMENT IN MEDICAL CARE

10. WE BELIEVE, that the best possible quality, quantity, availability, and distribution of medical care for our American people can only be secured by the creation of a

permanent, working, medical care conference composed of (1) the medical and allied health professions, concerned with medical services and (2) governmental agencies concerned with medical services.

JOINT PLANNING FOR MEDICAL CARE

WE BELIEVE, that such a joint cooperative conference effort on the part of medical and governmental agencies could improve the quality, quantity, availability, and distribution of medical care for all of the American people by jointly planning care for (1) the medical indigent and low-wage groups—by the supplemental aid of general tax funds; (2) by caring for those of moderate income—by voluntary health insurances covering hospital, medical, surgical, obstetrical, and all other medical care expenses and (3) by caring for those of ample income—as at present.

A PERMANENT DEMOCRATIC MEDICAL CARE CONFERENCE OF MEDICAL AND GOVERNMENTAL AGENCIES

WE BELIEVE AND RECOMMEND, that such permanent working conference on medical care should be forthwith immediately created either by (1) the A.M.A., (2) the Congress of the United States, or (3) the President of the United States, preferably by joint action of these three), to be composed of an equal number of official representatives of (1) the A.M.A and (2) the governmental agencies concerned with health services; and that the members of such conference be given equal powers of action to the end that the American people may be provided in our time with the best possible quality, quantity, availability, and distribution of medical care by concerted American democratic action with resultant peaceful solution of the medical care problems which concern us all.

News and Notes

The deaths of the following Fellows have been reported to the JOURNAL:

Dr. Edward S. Babcock, Sacramento, Calif., September 3.

Dr. Edward B. Weldon, Bridgeport, Conn., in August.

Dr. Charles G. Kerley, New York City, died at his home on Sept. 7, 1945, at the age of 82 years. He had been president of the American Pediatric Society and also a member of other medical organizations. He was a well-known teacher and practitioner of Pediatrics.

Dr. Edgardo Burgos, Vía España 112-A, Republic of Panama, has been appointed Diplomatic Minister from the Republic of Panama to Uruguay.

Dr. John P. Hubbard of Boston has accepted the position of Director of the *Academy Study of Medical Care*. Dr. Hubbard has just been released from three years of service as Colonel in the Army Medical Corps. Previous to his military service he was in practice in Boston and was on the staff of the pediatric department of Harvard Medical School. He had charge of the cardiac clinic at the Children's Hospital in Boston. Dr. Hubbard will take up his work as director at the office of the study at the Children's Hospital in Washington the middle of November.

At the last meeting of the Seattle Pediatric Society, the name of the Society was changed to Puget Sound Pediatric Society. The following members were elected officers for the current year:

President: Dr. H. T. Clay, Tacoma, Wash.

Vice-President: Dr. W. B. Seelye, Seattle, Wash.

Secretary-Treasurer: Dr. W. B. Chesley, Seattle, Wash.

The time of the meeting is the third Friday of each month.

The Pediatrician and the War

The following promotions have been reported to the JOURNAL:

Army

Captain Warren F. Belknap, Detroit, Mich., to Major
Captain Wilbur J. Fisher, Buffalo, N. Y., to Major
Captain R. J. McGillicuddy, Lansing, Mich., to Major
Major Jack Harrison, Chicago, Ill., to Lieutenant Colonel
Captain Irving Silverman, Edgewood, R. I., to Major
Captain George H. Wegman, Milwaukee, Wis., to Major

Navy

Lieutenant (sg) Jack Basman, Charleston, W. Va., to Lieutenant Commander
Lieutenant (sg) Harold A. Rosenberg, Jackson Heights, N. Y., to Lieutenant Commander

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The following have been released from service:

Dr. M. C. Carlisle, Waco, Texas
Dr. Samuel J. Hoffman, Chicago, Ill.
Dr. Dennis H. Kelly, Des Moines, Iowa
Dr. Noah Miller, Akron, Ohio
Dr. Philip A. Mulherin, Augusta, Ga.
Dr. Henry N. Pratt, Boston, Mass.
Dr. John R. Ross, Toronto, Canada
Dr. Norman Survis, New Rochelle, N. Y.
Dr. Harry A. Towsley, Ann Arbor, Mich.
Dr. Bernard Zuger, Brooklyn, N. Y.

Correspondence

London Hospital
London, England
August, 1945

It is, unfortunately, a very long time since your correspondent in England forwarded you an official letter. For this he apologizes, but it has been due to the war, and he himself was away from England and stationed in the Tropics for two years during the course of more than three years' military service.

On returning to civil life one is struck with the good nutritional condition of the children in this country. Rationing has been carried out most intelligently, and the Ministry of Food has been really a shining example of an enlightened ministry. There were many gloomy forbodings regarding infant nutrition at the onset of the war, and it is most gratifying to find that no fallng off in infant nutrition has been noticeable during the present war over here.

Lewis-Faning and Milligan carried out at Glossop a well-controlled series of observations which can, I think, be regarded as representative. During the period July, 1940, to July, 1942, these workers observed 482 infants throughout the first year of life and compared them with a similar group of 307 infants observed in the prewar period. It was shown conclusively that the former group had the advantage in regard to weight, length and rate of growth, and also a slightly lower wartime mortality rate. Apart from this carefully carried out piece of work, most physicians and nurses working among infants in this country would be prepared to say that no falling off in infant nutrition has been noticeable during the present war over here.

Regarding children in a older age group, the interim report of the County Medical Officer of Health of London for 1943 is of interest. On the basis of the School Medical Service returns, this report shows that the condition of London school children was better in some respects in the third and fourth years of war than in the prewar year of 1938. The proportion of children in whom nutrition was unsatisfactory was found to be 6.6 per cent in 1938, and this was reduced to 6.2 per cent in 1942 and 6.0 per cent in 1943. It is also a striking fact that despite housing difficulties associated with air raids and so on no widespread epidemics occurred during the early years of the war.

Evacuation of children to the country brought many problems in its train, largely of a psychological variety, and enuresis, for example, was frequently noted in these children settling in strange homes.

Delinquency among children has to some extent increased and has been attributed to the lack of paternal control, so many fathers being in the services and away from home.

Very early in the war the Government introduced a national dried milk which, in view of the difficulties of obtaining in the open market so many peacetime products, has helped to solve many troubles associated with the feeding of infants. They have also sponsored a Ministry of Food cod-liver oil compound, one drachm of which contains 750 international units of Vitamin D as compared with the 330 units contained in one drachm of the British Pharmacopoeal cod-liver oil.

One of our wartime arrangements which was spoken about by the Minister of Health at the last National Conference of Maternity and Child Welfare in June, 1945, has been the provision of day nurseries for children of war workers. These number no less than 1,500, with places for between 70,000 and 75,000 children.

The appointment by the Minister of Health of an advisory committee on mothers and young children, of which there is a medical and professional subcommittee, has been a progressive step conferring much benefit on the children.

The cooperation between the Ministry of Health and the British Paediatric Association which has occurred during the war and has gone from strength to strength, has been another great advance from a paediatric standpoint. It has resulted in various surveys being carried out and in the production of publications for the guidance of the medical profession, all of which have centered attention on current problems concerned with child welfare in its broadest aspect.

From what has been said it is apparent that at any rate the nutrition of children in this country has not suffered any setback during the war. Furthermore, the many difficulties that have had to be faced as a result of wartime conditions have stimulated paediatric activities in many directions with very gratifying results.

The British Paediatric Association held an excellent meeting this year at Rugby, the meeting actually taking place in the school itself, and we were glad to welcome Professor Struthers of Montreal, who is working over in Europe at present with United Nations Relief and Rehabilitation Administration. The programme was a good one and an abstract of the papers and proceedings will be published in due course in the *Archives of Disease in Childhood*.

KENNETH TALLEMAN.

Book Reviews

The Physiology of the Newborn Infant. Clement A. Smith, M.D., Springfield, Ill., 1945, Charles C Thomas, 312 pages. Price $5.50.

Dr. Smith has achieved a major success in writing *The Physiology of the Newborn Infant*, as it fills a much-needed niche in our literature on the subject of the neonatal period. The book is not only authentic on the subjects included, but is also written in an extremely interesting style, each chapter being provided with a summary which facilitates the understanding of the subject matter.

He takes up specifically the fetal and neonatal aspects of the respiratory system, physiology of the circulatory system of the blood, icterus, metabolism, and heat regulation, digestive tract, nutrition, kidneys, the endocrine glands, and immunology.

In each subject he has surveyed the literature up to the present time, and in his discussion of the recognized and controversial subjects alike, he has been specific enough so that the reader comes away from the book with the feeling that he has been brought up to date on many topics.

It is difficult to understand how any conscientious pediatrician can avoid using this book in his daily contacts with newborn babies.

The only possible criticism this reviewer could find with the book is the fact that it fails to mention some of the physiologic activities of the newborn which are perplexing to the clinician. I refer to the more ordinary evidences of activity, such as crying, appetite, and the technique of breast feeding.

These omissions in Dr. Smith's text in no way detract from the usefulness of the book, but it is hoped that in his future editions, he will add some of these more commonplace topics to his discussion.

C. A. A.

An Introduction to Group Therapy. S. R. Slavson, New York, 1943, Commonwealth Fund, 352 pages. Price $2.00.

Based on the recognition that man is a social animal, workers in the field of psychotherapy have experimented with group experiences as instruments of psychiatric treatment. There has resulted a new treatment method called Group Therapy.

The Jewish Board of Guardians of New York, which is a social service agency rendering child guidance service to children with personality problems, has experimented with this method since 1934. The author of this book directed the study and has formulated in a well-arranged manner an account of its development and achievements. The basic principles of all interpersonal therapy are affirmed and related to the practice of Group Therapy. Included are discussions of the choice and grouping of suitable patient-subjects, and case record illustrations of the function of the therapist and patient. The book will not attract the average pediatrist, because it is a technical treatise on a subject which requires for adequate understanding a more basic knowledge of psychotherapy than the pediatrist usually has acquired. For those with psychological insight, as well as interest in and elementary knowledge of modern child psychology, it will stimulate inquiry as to how modern pediatric practice may be modified to become more effective through clarifying the personal relationships between physician and patient. It will point out, too, indications for psychotherapy generally and criteria for referral of pediatric patients to psychiatric services. The book is recommended for a place in the library of every pediatric teaching center.

SENN

The Control of Communicable Diseases. Subcommittee on Communicable Disease Control of the Committee on Research and Standards, American Public Health Association. Price $0.35.

This booklet should be a companion to the *Report of the Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals of the American Academy of Pediatrics.* There is much that may never be needed, but that which is useful is well put, succinct, and authoritative. It deals with agents, methods of diagnosis, methods of transmission, methods of control of disease. The report of the American Academy of Pediatrics is mainly on therapy and hence this volume could be considered supplementary and of value to all practitioners.

JOHN A. TOOMEY

Comment

THE PEPPER BILL (S.1318)

Under the department Social Aspects of Medicine in this issue of the JOURNAL appear two communications discussing the Pepper bill which are "compulsory reading" for everyone. The articles by Drs. Richard M. Smith of Boston and Lee Forrest Hill of Des Moines were requested by the Editor of the column. Both approach the subject in a thoughtful way and discuss most of the moot points in regard to the bill, which will come up for consideration at the Academy meeting in Detroit in January.

These two communications carry out the ideas and intentions of the Editorial Board in establishing this department in the JOURNAL. The Editors are certain that a careful reading of the communications will help clarify the thoughts of every member of the Academy on the merits and weaknesses of the proposed act.

The Editors of the JOURNAL have resisted the temptation to comment on or discuss the points raised in the communications, in the belief that it is better for each individual to form his own judgment on the points presented.

THE EDITORS

INDEX TO VOLUME 27

A

Acceptance of foods and changes in adequacy of diets consumed, 393

Acidosis, production of, in premature infants by protein milk, 43

Adrenal gland, hemorrhage in; Waterhouse-Friderichsen syndrome, 281

Aegerter, E. E., and High, R. H., 343

Aldrich, C. Anderson, Sung, C., Knop, C., 428

—, —, —, Stevens, G., and Burchell, M., 89

Allergic child in camp, 75

American Academy of Pediatrics:
  governmental-professional relationships, problem of, 291
  news, 499
  news and notes, 87, 205, 298, 390, 499, 616
  report of committee on geographical distributions, 295
  meeting of executive board, 174
  treasurer, 383
  Thomas Benton Cooley (1871-1945), 497

American public health association, 621 (B. Rev.)

Anderson, John A., 68

Anemia of newborn, 265

Antibody reaction, heterophile, in infants and children, 540

Antiserum, treatment with, of acute laryngitis caused by hemophilus influenzae, 572

Arachnodactyly—unusual complication following skull injury, 583

Asphyxia neonatorum, use in, Greenberg modification of Flagg laryngoscope, 602

Atresia, congenital, of esophagus, surgical treatment of, 456

B

Bashinsky, Leo, 448

Behavior problems, avoiding, 363

Blair, Ruth, Greider, M., and Roberts, L. J., 393, 410

Blatt, Maurice L., Kern, M., and Kortuem, C. M., 71

Blattner, Russell J., Heys, F. M., and Harrison, M. L. K., 207

—, and Sung, C., 579

Blood and urinary excretion studies before and after dietary improvement, 418

Bloxsom, Allan, 447

Bone growth in congenital myxedema; use of serial roentgenograms of os radius in diagnosis and regulation of therapy during infancy, 229

Book reviews:
  Control of communicable diseases, 621
  Introduction to group therapy, 620
  Physiology of newborn infant, 620

Brennemann library, Joseph, 84

Bridge, Edward M., and Holt, L. E., Jr., 299

Brockway, George E., and Jacobs, M. H., 273

Brooksaler, Fred, 442

Brown, Willis E., and McIntosh, C. B., 323

Burchell, Margaret, Aldrich, C. A., Sung, C., and Knop, C., 89

C

Calcium and phosphorus, metabolism and clinical findings as influenced by certain feedings in rickets, study of, 521

Camp, allergic child in, 75

Cardiospasm in newborn, 565

Carman, Gordon A., Schapiro, I. E., and Walden, A., 288

Carr, Jesse L., 1

Ceballos, Alfredo, Frank, T. V., and Simpson, W. F., Jr., 281

Child, allergic, in camp, 75
  congenitally hypothyroid, generalized vaccinia and probable induced thiamine deficiency in, 595

Children and infants, diagnosis and management of severe infections in: review of experiences since introduction of sulfonamide therapy; IV. pneumococcus meningitis, 115
  heterophile antibody reaction in, 540
  comparative study and significance of tuberculin patch and Mantoux tests in, 245
  in an institution, results of providing a liberally adequate diet to, 393, 410, 418
  prevention of rheumatic recurrences in, by use of sulfathiazole and sulfadiazine, 516
  prognosis in acute glomerulonephritis in, 453
  salicylate therapy in rheumatic fever in, 59
  spinal cord tumors in: study of three cases of ependymoma, 315

Chorea in Negro race, 554
Clemens, Harry H., 267
Cohn, David J., Lawrence, G., and Gerstley, J. R., 521
Comment, 206, 504, 622
Communicable diseases, control of, 621 (B. Rev.)
Control of communicable diseases, 621 (B. Rev.)
Cooley, Thomas Benton, 497
Correspondence, 198, 618
Crying of newly born babies, 89, 428

D

Daniel, W. A., Jr., 554
Darrow, Daniel C., da Silva, M. M., and Stevenson, S. S., 43
Davies, John A. V., and Hutchins, G., 505
Davis, Joseph H., and Faber, H. K., 453
Diagnosis and management of severe infections in infants and children: review of experiences since introduction of sulfonamide therapy; IV. pneumococcus meningitis, 115
Diamond, Jerome, and Sennott, J. S., 540
Diet, liberally adequate, to children in institution, results of providing, 393, 410, 418
Diphtheria, percutaneous immunization against, 334
Diseases, communicable, control of, 621 (B. Rev.)
Docter, Jack M., 327

E

Edema with hypoproteinemia due to congenital defect in protein formation, 241
EMIC program, problem of governmental-professional relationships, as seen from experience under, 291
Ependymoma, study of three cases of: spinal cord tumors in children, 315
Erratum, 382
Erythema exudativum multiforme (Hebra) —bullous type, 465
Erythroblastosis fetalis, 353
  hemolytic disease of newborn, 249
  kernicterus: neurological sequelae of, 327
  neurological sequelae of: kernicterus, 327
Esophagus, surgical treatment of congenital atresia of, 456
Executive board of American Academy of Pediatrics, report of meeting of, 174

F

Faber, Harold K., and Davis, J. H., 453
Feedings, certain, in rickets, study of calcium and phosphorus metabolism and clinical findings as influenced by, 521
Ferris, Benjamin G., Jr., and Neuhauser, E. B. D., 589
Fischer, Golda, and McClure, L. E., 436
Fletcher, Mary W. Critz, and Harris, R. C., 465
Foods and changes in adequacy of diets consumed, acceptance of, 393
Frank, Thomas V., Simpson, W. F., Jr., and Ceballos, A., 281
Freud, Paul, Rhodes, A. W., and Weisz, A., 591

G

Galactosemia with hepatic damage, 338
Gerstley, Jesse R., Cohn, D. J., and Lawrence, G., 521
Glaser, Daniel F., 560
Glaser, Jerome, 75
Glaser, Kurt, and Lawrence, G., 492
Glomerulonephritis, acute, in children, prognosis in, 453
Glucose, saliva, quantitative study of, 71
Glycogen storage disease; observations on pathologic physiology of two cases of hepatic form of disease, 299
Gold, Harry, 546
Goldstein, Hyman, 245
Governmental-professional relationships, problem of, 291
Greenbaum, Jerome W., and Schick, B., 241
Greenberg, Lester J., 602
Greider, Marjorie, Roberts, L. J., and Blair, R., 393, 410
Gropper, Easton M., Lamanna, C., and Stewart, C. A., 595
Growth charts for use in pediatric practice, 215
  in weight and height, 410

H

Handelman, N. I., and Rotondo, C. C., 576
Harris, Ruth C., and Fletcher, M. W. C., 465
Harrison, Mary Lou K., Blattner, R. J., and Heys, F. M., 207
Hartmann, Alexis F., Love, F. M., Wolff, D., and Kendall, B. S., 115
Heart disease, rheumatic, with associated meningoencephalitis, 343
Height and weight, growth in, 410
Hemophilus influenzae, treatment with antiserum of acute laryngitis caused by, 572
  type F, meningitis caused by, 567
Heys, Florence M., Harrison, M. L. K., and Blattner, R. J., 207
High, R. H., and Aegerter, E. C., 343
Holt, L. Emmett, Jr., and Bridge, E. M., 299
Home, early period at; crying of newly born babies, 428

Horstmann, Dorothy M., 235
Hutchins, Gretchen, and Davies J. A. V., 505
Hypoproteinemia due to congenital defect in protein formation, edema with, 241

I

Immunization, percutaneous, against diphtheria, 334
Infancy, use of serial roentgenograms of os radius in diagnosis and regulation of therapy during; bone growth in congenital myxedema, 229
Infant, allergic, penicillin therapy of staphylococcus aureus hemolyticus infection in, 436
  feeding, further records of self-demand schedule in, 109
  newborn, cardiospasm in, 565
    hereditary skin defect in, 591
    physiology of, 620 (B. Rev.)
    with cleft palate, obturator (acrylic) for, 288
  staphylococcus albus hemolyticus meningitis in, 267
Infants and children, diagnosis and management of severe infections in: review of experiences since introduction of sulfonamide therapy; IV. pneumococcus meningitis, 115
  heterophile antibody reaction in, 540
  newborn, penicillin locally in eyes of, to prevent ophthalmia neonatorum, 447
  newly born, crying of, 89, 428
  penicillin treatment of pneumococcus meningitis in, 505
  premature, production of acidosis in, by protein milk, 43
  treatment of acute suppurative parotitis in, 589
Infections, in infants and children: diagnosis and management of, 115
Institution, results of providing a liberally adequate diet to children in, 393, 410, 418
Introduction to group therapy, 620 (B. Rev.)

J

Jackson, Robert L., and Kelly, H. G., 215
Jacobs, Martin H., and Brockway, G. E., 273
—, Taran, L. M., and Krautman, B., 59
Jordan, Robert G., Jr., and Turner, J. R., 572
Joseph Brennemann library, 84

K

Kaposi's varicelliform eruption, etiology of, 207
Kappes, Marion, 84
Kelly, Helen G., and Jackson, R. L., 215
Kendall, Barbara S., Hartmann, A. F., Love, F. M., and Wolff, D., 115
Kern, Maximilian, Kortuem, C. M., and Blatt, M. L., 71
Kernicterus: neurological sequelae of erythroblastosis fetalis, 327
Knop, Catherine, Aldrich, C. A., and Sung, C., 428
—, —, —, Stevens, G., and Burchell, M., 89
Kortuem, Cecelia M., Blatt, M. L., and Kern, M., 71
Kraft, Ruth, M., Trainham, G., and Pilafian, G. J., 97
Krautman, B., Taran, L. M., and Jacobs, M. H., 59

L

Lam, Conrad R., 456
Lamanna, Carl, Stewart, C. A., and Gropper, E. M., 595
Laryngitis, acute, caused by hemophilus influenzae, treatment of, with antiserum, 572
Laryngoscope, Flagg, Greenberg modification of—its use in asphyxia neonatorum, 602
Lawrence, Grace, Gerstley, J. R., and Cohn, D. J., 521
—, and Glaser, K., 492
Leonard, Martha F., 249
Leslie, John T., 265
Litchfield, Harry R., 353
Love, Frances M., Wolff, D., Kendall, B. S., and Hartmann, A. F., 115
Lupus erythematosus, acute disseminated, with seven-year recovery, 235
Lyon, R. A., Wolf, R. E., and Rauh, L. W., 516

M

MacLaggan, James, Mellinkoff, S., and Roth, B., 338
Mantoux tests, tuberculin patch and, comparative study and significance of, in children, 245
Maryland, counties of, program for medical care of medical indigent in, 384
McCammon, Robert W., and Woolley, P. V., Jr., 229
McClure, Laura E., and Fischer, G., 436
McIntosh, C. Berkeley, and Brown, W. E., 323
McLendon, P. A., and Simsarian, F. P., 109
Mecholyl bromide, treatment of congenital megacolon with, 484
Medical care of medical indigent in counties of Maryland, endorsed by medical and chirurgical faculty of Maryland, program for, 384
Medicine, social aspects of, 202, 384, 502, 606
Megacolon, congenital, treatment with mecholyl bromide, 484
Mellinkoff, Sherman, Roth, B., and MacLaggan, J., 338

Meningeal infection, congenital dermal sinus as source of, 79
Meningitis caused by type F hemophilus influenzae, report of case with recovery, 567
meningococcic, report of multiple cases occurring in same family, 576
pneumococcal, following streptococcal viridans meningitis, in same patient with recovery, 273
pneumococcus: diagnosis and management of severe infections in infants and children, 115
in infants, penicillin treatment of, 505
staphylococcus albus hemolyticus, in infant, 267
streptococcal viridans, followed by pneumococcal meningitis in same patient with recovery, 273
Meningoencephalitis, associated with rheumatic heart disease, 343
Milk, protein, production of acidosis in premature infants by, 43
Myositis ossificans progressiva, 348
Myxedema, congenital, bone growth in, 229

N

Negro race, chorea, in, 554
Neuhauser, Edward B. D., and Ferris, B. G., Jr., 589
Newborn, anemia of, 265
hemolytic disease of (erythroblastosis fetalis), 249
News, academy, 499
and notes, 87, 205, 298, 390, 499, 616
Nisenson, Aaron, and Patterson, G. H., 315

O

Obturator (acrylic) for newborn infant with cleft palate, 288
Oldham, Helen, Roberts, L. J., and Young, M., 418
Ophthalmia neonatorum, penicillin locally in eyes of newborn infants to prevent, 447

P

Palate, cleft, obturator (acrylic) for newborn infant with, 288
Parke, James G., 567
Parotitis, acute suppurative, in infants, treatment of, 589
Patch test, tuberculin, and Mantoux, comparative study and significance of, in children, 245
Patterson, George H., and Nisenson, A., 315
Patton, Edwin F., 532
Pediatrician, and war, 88, 205, 298, 392, 501, 617
proctological problems of, 532
Penicillin locally in eyes of newborn infants to prevent ophthalmia neonatorum, 447
therapy in ratbite fever, 442
of staphylococcus aureus hemolyticus infection in an allergic infant, 436
treatment of pneumococcal meningitis in infants, 505
unusual fulminating generalized staphylococcus infections treated with, 448
Peterman, M. G., 484
Phosphorus and calcium metabolism and clinical findings as influenced by certain feedings, study of, in rickets, 521
Physiology of newborn infant, 620 (B. Rev.)
Pilafian, Grace Jones, Kraft, R. M., and Trainham, G., 97
Pneumococcal meningitis following streptococcal viridans meningitis in same patient with recovery, 273
Pneumonia due to streptococcus viridans, 480
Poliomyelitis and recent tonsillectomy, 68
bulbar, tracheotomy in, 560
Practice, pediatric, growth charts for use in, 215
sedatives and stimulants in, 546
Pratt-Thomas, H. R., and Waring, J. I., 79
Problem of governmental-professional relationships, 291
Proctological problems of pediatrician, 532
Protein defect in formation of edema with hypoproteinemia, 241
Pseudohermaphroditism, adrenogenital, treated with stilbestrol, 323
Pyoderma, Kaposi's varicelliform eruption, etiology of, 207

R

Ratbite fever, penicillin therapy in, 442
Rauh, Louise W., Lyon, R. A., and Wolf, R. E., 516
Regime, self-demand, case history of twins breast fed on, 97
further records of, in infant feeding, 109
Reinhart, John B., and Venning, W. L., 480
Results of providing liberally adequate diet to children in institution, 393, 410, 418
Rheumatic fever, prevention of recurrences in, in children by use of sulfathiazole and sulfadiazine, 516
salicylate therapy in, in children, 59
Rhodes, Adrian W., Weisz, A., and Freud, P., 591
Rickets: study of calcium and phosphorus metabolism and of clinical findings as influenced by certain feedings, 521
Roberts, Dean, 384

Roberts, Lydia J., Blair, R., and Greider, M., 393, 410
—, Young, M., and Oldham, H., 418
Roentgenograms, serial, of os radius in diagnosis and regulation of therapy during infancy, use of, 229
Rogers, Edward S., 291
Roth, Bernard, Mellinkoff, S., and MacLaggan, J., 338
Rotondo, C. C., and Handelman, N. I., 576
Ryan, Kermit J., 348

S

Salicylate therapy in rheumatic fever in children, 59
Saliva, glucose, quantitative study of, 71
Schapiro, I. E., Walden, A., and Carman, G. A., 288
Schick, Béla, and Greenbaum, J. W., 241
Schneider, Wilmot F., 583
Sedatives and stimulants in pediatric practice, 546
Sennott, John S., and Diamond, J., 540
da Silva, Mauricio Martins, Stevenson, S. S., and Darrow, D. C., 43
Simpson, William F., Jr., Ceballos, A., and Frank, T. V., 281
Simsarian, Frances P., and McLendon, P. A., 109
Sinus, congenital dermal, as source of meningeal infection, 79
Skin defect, hereditary, in newborn infant, 591
Skull injury, arachnodactyly, unusual complication following, 583
Slavson, S. R., 620 (B. Rev.)
Smith, Clement A., 620 (B. Rev.)
Social aspects of medicine, 202, 384, 502, 606
Sodium sulfadiazine, subcutaneous administration of, 492
Spinal cord tumors in children: study of three cases of ependymoma, 315
Spock, Benjamin, 363
Staphylococcus albus hemolyticus meningitis in infant, 267
  aureus hemolyticus infection in allergic infant, penicillin therapy of, 436
  infectious, unusual fulminating generalized, treated with penicillin, 448
Status thymico-lymphaticus, 1
Stevens, Geraldine, Burchell, M., Aldrich, C. A., Sung, C., and Knop, C., 89
Stevenson, Stuart S., Darrow, D. C., and da Silva, M. M., 43
Stewart, Chester A., Gropper, E. M., and Lamanna, C., 595
Stilbestrol, adrenogenital pseudohermaphroditism treated with, 323
Stimulants, and sedatives, in pediatric practice, 546
Streptococcal viridans meningitis followed by pneumococcal meningitis in same patient with recovery, 273
Streptococcus viridans, pneumonia due to, 480
Sulfadiazine, and sulfathiazole, use of, prevention of rheumatic recurrences in children by, 516
  sodium, subcutaneous administration of, 492
Sulfonamide therapy, review of experience since introduction of; diagnosis and management of severe infections in infants and children; IV. pneumococcus meningitis, 115
Sung, Chieh, and Blattner, R. J., 579
—, Knop, C., Aldrich, C. A., 428
—, —, —, Stevens, G., and Burchell, M., 89

T

Taran, Leo M., Jacobs, M. H., and Krautman, B., 59
Therapy, group, introduction to, 620 (B. Rev.)
Thiamine, probable induced, and generalized vaccinia, deficiency in congenitally hypothyroid child, 595
Thymus, consideration of normal weight of, 1
Tonsillectomy, recent, and poliomyelitis, 68
Tracheotomy in bulbar poliomyelitis, 560
Trainham, Genevieve, Pilafian, G. J., and Kraft, R. M., 97
Treasurer, report of, American Academy of Pediatrics, 383
Tuberculin patch and Mantoux tests in children, comparative study and significance of, 245
Tuberculosis, cystic, of bone, in case of miliary tuberculosis, 579
  miliary, cystic tuberculosis of bone in case of, 579
Turner, J. Render, and Jordan, R. G., Jr., 572
Twins, breast fed on self-demand regime, case history of, 97

U

Urinary excretion and blood studies before and after dietary improvement, 418

V

Vaccinia, generalized, and probable induced thiamine deficiency in congenitally hypothyroid child, 595
Venning, W. L., and Reinhart, J. B., 480
Vinson, Porter P., 565
Vollmer, H., and Wegman, M. E., 334
Von Gierke's disease, glycogen storage disease, 299

W

Walden, Arthur, Carman, G. A., and Schapiro, I. E., 288
War and pediatrician, 88, 205, 298, 392, 501, 617
Waring, J. I., and Pratt-Thomas, H. R., 79
Waterhouse-Friderichsen syndrome, 281
Wegman, M. E., and Vollmer, H., 334
Weight and height, growth in, 410
Weisz, Albert, Freud, P., and Rhodes, A. W., 591
Wolf, Richard E., Rauh, L. W., and Lyon, R. A., 516
Wolff, Dorothy, Kendall, B. S., Hartmann, A. F., and Love, F. M., 115
Woolley, Paul V., Jr., and McCammon, R. W., 229

Y

Young, Marjorie, Oldham, H., and Roberts, L. J., 418

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INDEX NUMBER

Vol. 27 DECEMBER, 1945 No. 6

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TABLE OF CONTENTS ON 3rd COVER

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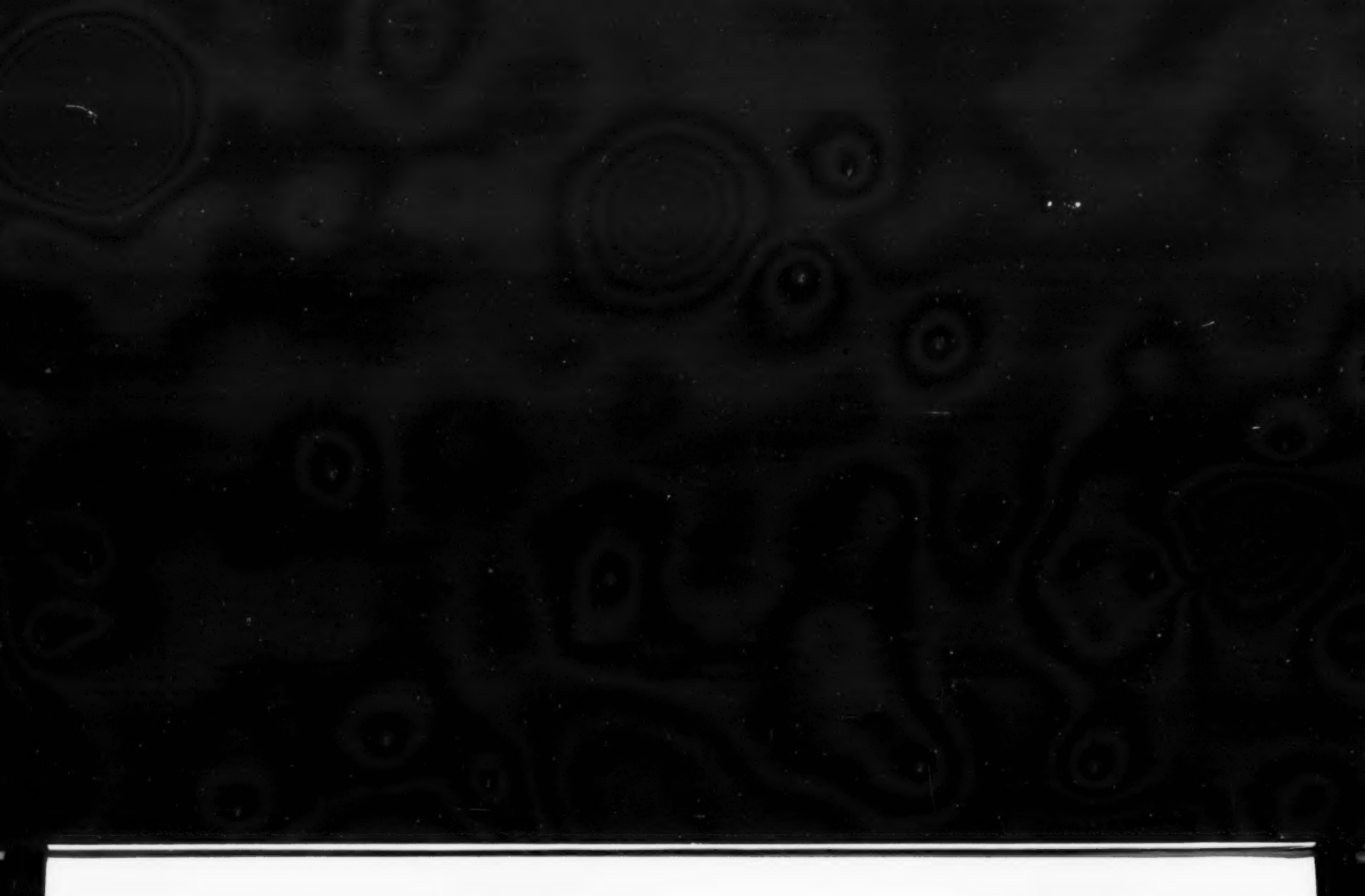
A&P

WHITE HOUSE EVAPORATED MILK

Fortified with 400 U.S.P. Units of "Sunshine" Vitamin D_3 per pint

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